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A MONTHLY JOURNAL DEVOTED TO THE PROBLEMS AND DISEASES OF INFANCY AND CHILDHOOD

Official Organ for
THE AMERICAN ACADEMY OF PEDIATRICS

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The Journal of Pediatrics

VOL. III SEPTEMBER, 1933 No. 3

Original Communications

PRESIDENTIAL ADDRESS
AMERICAN ACADEMY OF PEDIATRICS

S. McC. HAMILL, M.D.
PHILADELPHIA, PA.

IN HIS admirable presidential address delivered at our meeting a year ago, Dr. Morse set forth most beautifully and comprehensively the relationship that the Academy should bear to the health and welfare problems of the child and the unusual opportunities offered us as its fellows to render a high service to humanity. I would like nothing better than to repeat the substance of his address, but it is not in my power to handle it with the skill and finesse that did Dr. Morse.

The Academy is just emerging from the tender age of infancy and is celebrating its third birthday. Despite its youth it can point with definite pride to some real accomplishments or, perhaps one might better say, to very definite progress which augurs well for future accomplishment.

It may not be amiss, therefore, to stop for a moment to consider how far we have traveled.

The Academy came into being just as the White House Conference was completing its labors. The Conference undertook the prodigious task of ascertaining what was being done throughout the country for the health and protection of the American child, what were the gaps in the program, and how these gaps could be filled. The first two of these objectives were reasonably well covered but the third from lack of time was scarcely touched.

However, one very vivid fact that impressed itself upon the participants in the Conference was that, if we could bring about a full and intelligent application of the knowledge we already possess, the gaps in our program for the health and protection of the American child would be considerably reduced.

Annual meeting, Chicago, June 12, 1933.

Due to the clear vision of our secretary in laying the foundation for its activities the Academy has builded well to meet this important need.

We have created a number of committees which, functioning properly, should have an important educational influence in the fields they represent. They should make themselves fully conversant with their subjects and make that knowledge available to the agencies working in these various fields throughout the country. Although time does not permit a detailed consideration of all the committees I would like to draw your attention to outstanding features of the work of certain committees, the need for alteration of purpose or nomenclature for others, and future opportunities for still others. The Committee on Pediatric Education has done an admirable piece of research in its field, which it is continuing and which is being made of practical value to the medical schools of the country.

The Committee on Hospitals and Dispensaries issued a most searching and valuable questionnaire to the children's hospitals of the country. Through the interest and cooperation of the Fellows of the Academy all of these questionnaires save one have been returned fully answered. It is the first time such complete information on this subject has ever been assembled. This material is being tabulated and studied. From it will evolve a picture of the children's hospital situation which will enable us to evaluate the services of these institutions and be better qualified to advise intelligently regarding them.

As Dr. Morse said in his address, "Committees are of no use unless they do something."

Some of our committees have a rather limited field of action and it might be worth while for the Executive Board to consider whether some of them may not be advantageously eliminated. There is probably no further use for the Committee on Relations with the White House Conference. The Conference has ended and its follow-up committee has disbanded. However, under a somewhat altered title it might well serve a useful purpose. There was a vast amount of valuable information collected by the Conference. Unless someone carefully reviews the transactions of that Conference and extracts the material that has practical application, there is grave danger that it will remain buried in the tomes which embody it and never be put into action.

There would seem to be a very important service for the Committee on School Health and School Health Education. Both of the subjects included in this title are under criticism. We all know how inadequate is the health supervision of the school child the country over. We also know that this service is under severe criticism by the rank and file of the medical profession on the ground that it infringes upon the prerogatives of the physician.

There certainly should be some agency engaged in a study of this entire problem to determine its objectionable features and evolve a plan by which they can be overcome.

There is a prevalent impression that education in health, as given in our school systems, is unsatisfactory. To determine whether this impression is justified should be our function. We certainly should know whether instruction in the important subject of health protection is being intelligently and effectively carried out in our school systems.

The Committee on Mental Hygiene would seem to have not only an important but extremely interesting function. The question of the training a medical student should receive in psychiatry to enable him to cope with the behavior problems he will meet in practice; a study of the misleading literature that is being fed to young mothers and the means of combating its disturbing effect, and many other interesting points offer opportunity for this committee to do an effective work.

The Executive Board might also consider whether its committees are founded on the most efficient and effective basis possible. There are two kinds of committees which usually function well. One that is headed by a chairman who has a full knowledge of, and is vitally interested in, the subject the committee is created to consider. In such committees most of the work, however, is done by the chairman. The other is the local committee which has opportunity to bring its membership together frequently.

Committees of national organizations whose membership is widely scattered and who are without salaried executives, if dealing with subjects requiring constant and continuous consideration, are rarely effective. The work of the Academy committees is continuous and their membership widely scattered. The purpose of this latter point is easily evident. The Academy naturally desires to stimulate the interest and use the knowledge and ability of all of its members—a very important consideration—but from the standpoint of getting work done I am not sure the present committee plan is wise. Is it not possible to accomplish the desired result by increasing the membership of these committees, retaining an adequate geographic distribution but at the same time selecting in the community in which the chairman resides a group of four or five members who can get together frequently and support and advise the chairman? The results of the studies of the local groups could readily be submitted to the other members for review and criticism.

I believe further that it would be well for the Executive Board to consider the advisability of granting each of its committees a small stipend for occasional secretarial work and necessary postage, such an allowance to be based on evidence of serious activity on the part of the committee.

If such a course, or some other modification of the present plan, is followed and committees still fail to function, it would seem that the Academy should give careful consideration to the advisability of using other avenues through which to accomplish its purposes.

Our admirable Journal, which has had an almost unprecedented career in the first year of its existence, constitutes an excellent medium through which to extend our educational function.

May it not be possible for the Journal to lay more stress on the social aspects of medicine? The fields of sociology and preventive medicine are so interrelated and each dependent so much on the other that it has seemed to me we might advantageously use the columns of the Journal for freer discussion of these interrelated problems. Can't we also lay more stress upon the protection of health? The studies of the White House Conference showed a woeful lack of application of protective procedures. They report that a very small percentage of the children had been vaccinated against smallpox or protected against diphtheria, and still fewer had had health or dental examinations. Certainly we are the logical body to popularize these important procedures and the Journal should be a useful medium for accomplishing these results.

It was stated in the first issue of the Journal that "it is the intention of the editors to make it as broad and inclusive as the field of childhood itself."

We cannot expect the editors alone to attain this much desired goal. There are certainly many members in the Academy who are interested and experienced in these fields who could and should contribute. There are also many outstanding men and women in the social workers group who are keenly interested in the medical aspects of their problems and who could be induced to contribute to the columns of the Journal.

I am wondering whether the members of the Academy have responded as fully as they might to the appeal of our editors for material for the section of the Journal reserved for "News and Notes." I know that it has been the hope of our editors that this might become a very useful and interesting column. I would like to urge upon you the importance of doing everything in your power to make the Journal what I believe it can and should be, the most interesting and helpful forum for pediatric discussion in the country.

As I have reviewed, with great interest, the activities of Region II and those of the various state committees that have organized, I have become convinced that the regional and state committees offer a most effective avenue through which to accomplish many of our aims and purposes.

There are certain very definite needs we must meet and a number of obstacles we must overcome in the field of practice. The public is demanding that active measures be taken to protect the health of chil-

dren. Dr. Morse has pointed out that the public "will see to it that they are taken." As a matter of fact they are "seeing to it." The majority of us have been indifferent to this trend.

Our preventive clinics, our health centers, our state and municipal health departments, and to a less extent our hospitals, all of whose free services should be entirely restricted to the care of the indigent, are daily opening their doors wider to those who can afford to pay.

The medical profession is largely responsible for the fact that our potential pay patients are taking unfair advantage of this. We have been fully conscious of the fact that for years the public has been plied with propaganda urging upon them the importance of health protection. This propaganda has come from sources they respect and the public has been waiting for the physicians to offer them this protection. The profession at large has not equipped itself to render this protection, and those who are prepared have not had the courage to urge the value of health examinations and the importance of preventive procedures. The natural result is that the public has sought these services where they can be had.

We naturally object to this procedure, but what are we doing about it? Aren't we merely standing on the sidelines and futilely shouting our protests? Have we developed a plan to *check* this trend?

The Academy through its state committees has an unusual opportunity to put effective plans into action. The New Jersey committee has adopted a procedure which promises to be most effective. After careful consideration Pennsylvania decided to copy this plan with certain modifications. For illustrative purposes I shall refer to this Pennsylvania plan in some detail.

It calls for a state committee with county units to be under the auspices of the state medical society. The officers and trustees of the Medical Society of the State of Pennsylvania were overtured by the Pennsylvania Academy Committee with the request that they accept the responsibility of creating such committees in Pennsylvania.

About this time the Governor of Pennsylvania called a conference in Harrisburg to consider the best means of combating the rapidly increasing malnutrition among children that was being reported to the Emergency Relief Board, which at that time was feeding 450,000 families, including almost a million children.

At this conference a member of the Academy Committee, having in mind the proposal put before the state medical society, suggested that a state-wide Emergency Child Health Committee with county units be organized at once. This proposal was adopted and the stage was immediately set for carrying out the program that had been submitted to the officers and trustees of the state society.

A Planning Committee was organized, having in its membership the president, president-elect and secretary of the state medical society,

a representative of the state Academy Committee, together with representatives of the state departments of health and welfare, and three outstanding laymen.

This committee developed a program which, briefly outlined, called for the creation of the proposed state-wide committee with county units. This committee was to have in its membership representation from every state-wide agency, public and private, that was interested in the health and welfare of children, including an official representative from the State Academy Committee, together with several outstanding lay members.

As organized the committee consists of two honorary chairmen (the governor one of them and the president of the state medical society the other), a medical chairman, two vice-chairmen, an executive committee, and an advisory committee of pediatricians. Incidentally this latter committee is made up exclusively of members of the Academy of Pediatrics who are also members of the Pediatric Section of the State Society.

The organization of the committee, the selection of its personnel, the development of the plan of procedure and the carrying out of the work, was placed in the hands of the state medical society.

The organization of the county committees follows exactly that of the state committee. The county societies assume the same responsibilities in relation to these committees.

All appointments to membership in both the state and county committees are made by the governor on recommendation of the president of the state medical society. This has a very definite psychologic value.

It will be seen from the foregoing that both the state and county organizations bring together under medical leadership all of the agencies working in the state and the counties in the interests of children.

This is a type of organization which we believe opens the way for solving many of the problems that have been disturbing us.

A group of physicians, representatives of publicly and privately supported health agencies and representatives of the lay public—a group which should occupy an authoritative position in the state and its counties—are sitting down together planning the best procedure to follow for the protection of the health of the state's children in this very serious crisis. They are discussing the differences and the misunderstandings that have existed in the past and developing plans for their avoidance in the future—a procedure in cooperation that to my knowledge has not been accomplished anywhere heretofore. They are coordinating the work of the various agencies so that duplication will be eliminated and they are stimulating each other to more effective effort.

We hope through the medium of this closer cooperation and better understanding to persuade all agencies, both public and private, to re-

strict their services to the definitely indigent groups. This calls for a new attitude of mind not only on the part of the agencies but also on the part of physicians. The latter must be prepared to render the services in health protection to those who, they believe, should be refused this service by the clinics. This will probably entail an adjustment of fees to meet the economic circumstances of this group. One of the first important points to establish is the economic basis on which free treatment should be refused. This is a wholly unsettled point but one which these county committees, with their varied representation, should be able to determine. They can also develop a plan satisfactory to the medical profession for the economic rating of those who are refused free treatment so that they may be referred to their physicians with a definite recommendation as to the fee to be charged. Such a system is in action in the Philadelphia schools in respect to eye patients and is working very satisfactorily. It was put through under the auspices of the Philadelphia County Medical Society. The reactions we have had from physicians in several of the counties of Pennsylvania have convinced us that such a plan is feasible and would be acceptable.

As has just been said, the physician must be equipped to make the necessary health examinations and to apply the essential protective procedures. We dare not put ourselves in the position of objecting to the giving of a service by others which we ourselves are not prepared to render.

This point has been taken into consideration in the development of our work in Pennsylvania. Realizing that a health examination must be the basis on which to determine the health and nutritional status of the children we are called upon to protect, the Pediatric Advisory Committee has prepared a health examination form which is officially endorsed by the state medical society. It is so formulated as to require consideration of the entire child. We feel that the making of these examinations by many physicians will have a very definite educational value. To supplement this educational feature we have prepared an explanatory leaflet which is given to each examining physician. In addition we are sending pediatricians to the County Societies that request it to discuss with them the subject of health examinations.

The State Committee of the Academy is at present engaged in formulating a plan for definite courses in preventive pediatrics to be put into operation in the autumn.

We hope through these various avenues not only to equip the physician for this service but also to stimulate his active interest.

There have been two developments in the course of the emergency work in Pennsylvania that are especially gratifying. One is the eagerness with which lay organizations and individuals have accepted medical leadership, and the other is the extraordinary cooperation we have

received from the medical profession. Of course we have had individual objectors, but up to the present time every county medical society, save one or two, that has been approached, and this includes more than three-fourths of them, has accepted the program and almost always with enthusiasm.

The officers and trustees of the state medical society are so imbued with the value of the present organization that they plan to continue it in a somewhat modified form after the present crisis is over.

While this work has been organized to meet an emergency, the procedure that was followed in its formation would have been successful even had the emergency not existed, just as has been that of the New Jersey plan. The officers and trustees of the Medical Society of the State of Pennsylvania were in process of endorsing the original proposal of the State Academy Committee when the call for the emergency committee came to them.

The emergency merely made it easier of accomplishment and earlier of realization. In other words, the emergency created the psychological moment for the development of the work. That emergencies do play a very definite part in the development of new lines of procedure in public health is evidenced by the fact that the first state health department ever created was the result of a serious emergency.

I have described the Pennsylvania procedure in some detail because I believe it creates a feasible and practicable plan to offset or cure many of the evils that have been referred to above, as well as to provide a very much needed procedure in health protection.

The State Academy Committee is not numerically strong enough in any state to make its direct efforts felt in a statewide program. On the other hand, much can be accomplished if the state committees will serve as initiating groups in interesting the state and county medical societies and the various health agencies in a manner similar to that which has been followed in New Jersey and Pennsylvania.

Through such procedure we have opportunity to make the Academy a potent force in the field of child health throughout the nation. From the date of its foundation I have been deeply impressed by the possibilities of the Academy in the relatively undeveloped field of preventive pediatrics. The measure of success we will attain depends entirely upon the seriousness and enthusiasm with which the Fellows of the Academy enter the service. It is in our power to lead the way. Let us not falter!

THE DEVELOPMENTAL HEALTH EXAMINATION

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THE NATURE OF A DEVELOPMENTAL HEALTH EXAMINATION

IN PREPARING and interweaving accounts of the developmental growth of children for the White House Conference it was a comparatively easy task to differentiate deviations from satisfactory progress so gross that they fall under the caption of ill health for it is within the training and experience of every physician to recognize frankly pathological states which require the application of restorative medicine. It was however quite another, and indeed a far more difficult, problem to determine standards of optimum developmental growth. One clearly could not take the maximum as a criterion for there are aberrancies of excess as well as of deficiency. Progress, moreover, must be balanced. Physical growth may not outstep physical maturation. Nor must the physical aspect of developmental growth fall out of line with mental expansion. Mental expansion must be aligned with emotional stability. Experience has great influence in the transformation of capacity into ability. Interests play their part. Talent, that most unpredictable of all human traits, cuts right across the path of progress and brings its own influence to bear on the developing personality. In attempting to outline healthy developmental progress we have then to consider quite other features than those which determine medical health.

Medical health is essentially a record of status: developmental health is essentially a record of progress. That is why the serial examination is necessary for the latter determination.

Developmental health presupposes absence of any gross deviations from medical health. Hence the developmental health examination may include but does not necessarily imply a medical health examination. In my report on the assessment of physical status[8] to the White House Conference it was necessary to build such program of developmental health as we then had upon the routine medical examination. Since that date, the Developmental Health Inquiry of the Associated Foundations in Cleveland has provided the opportunity of outlining in more definite terms those assessments which give us information upon developmental progress. In the Cleveland experimental study these are subdivided into physical, orthodontic, psychological and sociological groupings. Under the physical heading come measures of growth, of maturation, of posture and of nutritional progress. The

From the Laboratory of Anatomy, Western Reserve University and Associated Foundations.

orthodontic group includes assessments of facial growth, of dental calcification and eruption and of the proper development of nose and nasopharynx. In the psychological group are estimates of muscular power and coordination, of personal social reactions, of reasoning and the handling of factual material, of mechanical intelligence and ability, of self-reliance and emotional stability. The sociological determinations are those of socio-economic stability and advantages, of family integration and group acceptance.

Although we are still in the exploratory phase of the subject and many of these measurements are not yet simplified so that they can be effectually and economically put into practice on a large scale, the day is not distant when an adequate developmental health assessment will be devised of so simplified a character that it can be applied in the course of regular practice. And some of the tests at least may even now be utilized with distinct advantage by the pediatrician.

THE CONDUCT OF A DEVELOPMENTAL HEALTH EXAMINATION

A. *Physical Growth.*—The significant measurements of physical growth are: weight, recumbent length, stature, height of left iliac crest from floor, greatest breadth over iliac crests, bitrochanteric diameter, and length of tibia from articular edge of inner tuberosity to tip of tibial malleolus. Chest measurements and expansion, it must be observed, like vital capacity, fall under the medical examination. The difference between stature and recumbent length gives a measure of posture. The height of iliac crest gives the proportion of leg length to stature. Bi-iliac and bitrochanteric diameters are really measures of maturation. Tibial length is the most easily obtained measure of growth in a limb bone for comparison with stature.

B. *Physical Maturation.*—For the estimation of physical maturation roentgenograms are necessary. Between birth and fifteen years these should comprise anteroposterior of left hand and wrist; dorsoventral and lateral of left foot and ankle; posteroanterior of left knee. All four can with care be taken on two 8 by 10 inch films. Between twelve and fifteen years an anteroposterior roentgenogram of the elbow is of assistance but not really necessary. Between fifteen and twenty years elbow and foot are not required. At that period of adolescence the hand and knee roentgenograms should be taken on a single film and a second film used for shoulder. The details of technique and interpretation are given in my account of roentgenographic appraisement for the White House Conference.[9]

C. *Orthodontic Appraisement.*—This is a somewhat specialized assessment the details of which have been fully set forth by my colleague, Dr. B. H. Broadbent,[2] and its application to the study of nasal passages and adenoid growth will shortly be published by Dr. H. C. Rosenberger.[5]

D. *Psychological Assessment.*—The psychological progress is ascertained by tests appropriate to the age and type of mental expansion on which information is desired. For children of eighteen months or less the Gesell tests are of service. From two to six years the Merrill Palmer tests give a measure of intelligence expressed in performance. Motor tests are employed to give a measure of muscular coordination. The Binet test of course measures intelligence expressed vocally, though it assesses only pure reasoning and the handling of factual material. Other tests of useful character are the man drawing test; the Minnesota mechanical abilities tests and paper form board; the Ascendancy-Submission test; the Woodworth-Mathews personality rating and the Bernreuter Inventory.

E. *Sociological Appraisement.*—The sociologic investigation is still less ready for general application though the Sims socio-economic rating scale gives some measure at least of socio-economic advantages.

THE APPLICATION OF ROUTINE DEVELOPMENTAL HEALTH DETERMINATION TO PEDIATRIC PRACTICE

Accepting the fact that, so far, the sociological and orthodontic tests are insufficiently simplified for general use and that psychological assessment demands special training and is therefore as yet very restricted in its applicability to routine practice we still have the measures of physical appraisal which can be utilized at once and interpreted with fair assurance after a little experience. The technique is simple, the cost low and the interpretation not too difficult to be mastered by the busy practitioner.

I. THE SIGNIFICANCE OF PHYSICAL MEASUREMENTS

The physical measurements selected above will determine the tempo of actual increment in size. They should be compared with the White House Conference tables or those prepared by R. M. Woodbury for children under six years[12] and for older white children by Baldwin and Wood[1] or for colored children by Royster and Hulvey.[6] It is true that the Woodbury standards are rather low but we find in practice so many children whose status in physical growth is mediocre though their progress between examinations is satisfactory, that the Woodbury standards are really of great practical advantage for they rarely compel the physician to explain to a parent why the child's progress is not at least average in amount. There are, however, far more important deductions to be drawn from growth progress than the simple satisfaction of parental ambition. In a way increments of weight, if paralleled by proportionate increments in stature during the infancy and preschool phases, are measures also of physical maturation. At least the two phases of developmental growth are very closely correlated. And the mental development, in the majority of

healthy children, keeps pace with the physical growth. It is our experience that the child who has, by his third birthday, reached the stature and weight of an average five-year-old child as designated on the Woodbury tables, will also have reached approximately the five-year stage in physical maturation and mental progress. It is important to realize that whereas the body takes some eighteen to twenty years to reach adult growth, the brain has practically reached adult size by the sixth birthday. The changes in cerebrum attained after that date seem to be connected with the development of association centers and connections which reduce the depth of the fissural pattern.[3]

The psychologists tell us that the type of mental development changes fundamentally after the age of six years so that, instead of being an elaboration of capacity, it takes the form of a training in ability.[4]

Children who grow and mature rapidly before the age of five years must not be expected to continue at this tempo during the grade school period. There is, as it were, a plateau of progress which may be attained early or late. Those who reach it early diminish their rate of progress so that by five years there is a greater uniformity of size and maturation than at any earlier period excepting perhaps the first birthday.

After the stage reached between five and six years one may expect, during the grade school period, another phase of increased growth velocity lasting a year or two and expressed in children of good physical constitution rather earlier than in those of less satisfactory developmental health but showing itself in all children under the age of nine years. It is followed by diminished activity of growth during the period of approximately nine to eleven years. After this renewed vigor of growth sets in with the approach of adolescence.

Allergic children begin to change their type of growth progress about the age of seven years. Their stature increases out of proportion to their weight and the lean "bean-stalk" type of child begins to show itself. Kretschmer's types indeed are obvious during adolescence but their body form is already demonstrable at a much earlier age.

The early adolescent growth in stature, when expressed on the Baldwin-Wood or Royster-Hulvey standards, is more vigorous in boys than in girls but this is largely a matter of comparison with adult stature. The girl reaches her full height at an earlier age than the boy and therefore the increase in pelvic dimensions is more obtrusive in the girl at this stage. The increase in bitrochanteric diameter is partly due to accumulation of panniculus but is also produced by growth of femoral neck and lateral displacement of great tuberosities of the femora. It occurs rather earlier than the increase in bi-iliac diameter which, in its turn in girls, precedes and accompanies the establishment of the menstrual periods.

Relatively late occurrence of the menarche seems to imply delay in the cessation of stature increase and in union of the epiphyses; girls of this type grow taller than those whose menarche supervenes early, largely because growth is possible in them over a longer period of the second decade.

Stature increase in boys remains possible through a greater part of the second decade and their adult height is much greater on the average than that of girls, a sex difference which is distinctly anthropoid in character since it is far more characteristic of higher primates than of lower primates or non-primate mammals.

In all interpretations of stature and weight increase the family line characteristics must be reckoned with but nutrition and medical health play a significant rôle as is well seen in Mitchell's studies of Porto Rican children compared with those of the continental United States. In general, stature and weight increments beyond the average are a rough measure of constitutional health but, also generally speaking, they are of less significance in this respect than the roentgenographic appraisement of physical maturation.

II. ROENTGENOGRAPHIC APPRAISEMENTS

The roentgenograms suggested earlier in this survey shed a very significant light on developmental growth and health if carefully studied and properly interpreted. They give measures of mineral reserves and therefore of constitutional fitness, of constitutional vulnerability, and of physical maturation. These three features should be considered separately.

The Estimation of Mineral Reserves.—Without going into detail on the subject of mineral reserves it may be recalled that Sherman has emphasized the iron-rich, calcium-poor status of the infant.[7] This, however, has no necessary relation to blood-calcium studies since blood-calcium is merely calcium in transit without indication of its source or destination. Its significance for bone growth, neuromuscular progress and kidney function are, however, evident enough. The chief depots of mobile calcium are the metaphyses of the long bones of the limbs and the bones of the hands and feet. Demineralization from whatever cause, as in the osteoarthritic period, in pregnancy, in adolescence, or in infancy, makes its appearance chiefly in these areas. In the dimineralization of rickets, epiphyses or carpal bones already ossified may lose their calcium so that they appear as "ghost centers" in the roentgenogram. We are not concerned, in developmental health, with extreme conditions such as this, but with the fluctuations observable in the mineralization of the skeletal depots. Epiphysial ossification in infancy and early childhood is but one phase of this mineralization study. Breast-fed babies show a slower progress of epiphysial ossification, whether or not cod liver oil is administered, than babies

fed upon a non-maternal diet. During the period of adjustment to non-maternal diet the progress in epiphysial ossification is quite slow but a rapid increase in progress is a measure of the completion of adjustment. Babies on cow's milk with cod liver oil show more vigorous progress in the epiphysial ossification schedule between six and twelve months than babies upon other formulae. Boys tend to a slower progress than girls in epiphysial ossification in the latter half of the first year but make up for this tardy progress once they have passed the first birthday. These distinctions still require much further investigation but they are quite evident in a carefully controlled study. Accompanying them can be seen fluctuations in the mineralization of cancellous texture and of compacta though no adequate measures of quantitative determination have yet been devised. The fluctuations are so great that quantitative methods are not necessary for their recognition.

Demineralized infants maintain their functional progress as determined by tests of the Gesell type on motor responses, motor adaptability, and on personal social responses, and even in physical growth for some weeks, though, in a while, they fall behind in the motor and adaptive responses, and, somewhat later, in personal social responses. There is a distinct change in behavior: they become restless, irritable, apprehensive, and querulous. Once these behavior changes have appeared the replenishing of the skeletal depots will not be accompanied at once by a return of serenity in behavior, though the motor responses recover very quickly and often will promptly improve on the administration of an adequate dose of cod liver oil.

The demineralized infant is not necessarily sick though disturbances of an exudative or allergic type readily supervene. When that happens the child has passed from the fluctuation of developmental health to the decompensation and failure of reserves culminating in medical ill-health.

The vitamin ration, especially of A, B, and G seems to be closely associated with mineralization and the maintenance of constitutional health in infancy. I do not emphasize vitamins C and D, adequate doses of which are usually provided.

The rôle of demineralization as expressed in roentgenograms and affecting developmental growth in childhood cannot be touched upon in this survey which is designed merely to open the subject.

The Recognition of Constitutional Vulnerability.—The determination of damage suffered in constitutional health as the result of an infectious disease or other disturbance of medical health is often a matter of considerable import. The parental measure of a child's actual illness is frequently determined by the resultant disturbance of household routine. But in the absence of evident sequelae we have no adequate measure of the real constitutional setback. The lines of in-

terrupted growth evident on roentgenograms, especially between the third and fourteenth year, emphasized by Park, of Hopkins, give not only an estimate of the severity of the impact upon developmental growth but also of its date. This can be determined easily within a month of the occurrence if the bodily growth increments are known from serial developmental health examinations. Further, the length of time which the transverse line or "scar" remains is an indication of severity, for the longer it takes the bone to remodel its architectural pattern to eliminate the mark the greater the constitutional disturbance. There is some selective activity in these markings on the bones, for the lower tibia seems to bear the brunt of dietetic disorders, especially those of minor grade; whereas the lower radius, lower femur, and upper tibia are more often scored by the effects of the exanthemata. Much more could be said on this subject if space permitted even though the full story is by no means yet understood.

The Assessment of Physical Maturation.—It has previously been mentioned that below the age of five years physical measurements give a fair indication of the progress of development, or as the theme is better expressed, of progress in maturation. During the grade and high school periods, however, physical measurements express growth only, as increase in dimensions. They do not, except in pelvic dimensions, possess any relation to bodily maturation. To determine progress in this aspect of developmental growth roentgenograms are necessary. During the grade school period extension of ossification into the cartilaginous epiphyses and, during the high school age, epiphysial union permit determination of the stage attained in progress toward maturity of the skeleton. Empirically this progress is found to be closely related to general bodily maturation. The details of roentgenographic appraisement have been outlined in the White House Conference reports.[9, 10] Measurement of carpal areas, resorted to by many workers, is an effort in this direction but unsatisfactory in practice, since no adequate standards of measurement are possible in that portion of the skeleton which is one of the most susceptible to disturbance as a result of ill-health or nutritional deficiency. Standards of progress in maturation, other than those in the White House Conference reports, suffer from lack of precision since they presuppose a range of individual variation. Individual variation does indeed occur when the maturation stage is matched against chronological age but obviously no precise determination can be made upon a scale involving range any more than upon any other scale the graduations on which are blurred and indefinite. Actual practice in rating of roentgenograms in terms of the details of penetration or of epiphysial union alone can give confidence in this new and exact instrument for measuring physical maturation.

MEASURES OF SUPERIORITY

It is a simple matter to define a child as tall or heavy for his age, a child who looks old for his years, or a child with a high I. Q. But it is the discovery that physical maturation can be exactly determined which has rendered possible the intimate correlation of physical growth and mental expansion. A child may be tall and slender and high in Binet rating as most allergic children over seven years actually are, but until the physical maturation progress has been measured we have no adequate conception of the child's actual status. A child may be tall or short for his age but the stage reached in his physical maturation is the really significant factor in determining the more subtle personality traits which interplay with the mental expansion. A superior type of child, that is a child who has had the advantages of good nurture, adequate socio-economic advantages, and reasonable freedom from disturbances of health and of developmental growth, is tall for his age; of weight a little beyond the average for his height; of physical maturation several months or even two years above the mediocre mean for his years; and of a psychologic rating easily in advance of the average for his age. Harmonious superiority implies an approximate equality of advancement in all these features. Disharmonious superiority or precocity is the result of unequal progress in which one feature far outstrips the others.

RETARDED AND PATHOLOGICAL DEVELOPMENTAL GROWTH

The distinction between retarded and pathological developmental growth is evident even when it cannot be defined. Many girls and still more boys are tardy in entering their adolescent phase but, given time, they will make good the delay the only permanent objective result of which is an increased stature, though there are definite personality modifications and traits which may become permanently impressed upon the individual. A pathological interference with adolescent progress is recognizable in character of subcutaneous tissue, in body proportions, in personality traits as well as in the fact, ascertainable at last, that time alone does not suffice to eliminate the handicap to progress. For such children treatment is necessary. This should be directed toward the reestablishment of metabolic integrity rather than specific medication for growth stimulation. A good example is given by Dr. Priscilla White's diabetic children.[11] These children retarded, both in physical growth and physical maturation, at once began to repair both aspects of the deficiency when they were placed on regular doses of insulin. A similar and more generally recognized type is the hypothyroid child. There are, however, many children subthyroid in diathesis, not retarded enough to merit the definition of hypothyroidism. Roentgenographic determination of physical maturation permits the recognition of many lesser degrees of retardation

more temporary in character and usually self-rectifying in time, following the exanthemata and other forms of health disturbance. Infantilism is one of the most intractable of these forms. Further consideration of this aspect of our problem would bring us back into the medical health examination from which we sought to free ourselves in elaborating the theme of the developmental health assessment.

SUMMARY

1. A medical health examination is an assessment of constitutional status; a developmental health examination is an assessment of specific progress in physical growth and maturation, in mental expansion, in emotional stability, and in other aspects of normal healthy childhood.

2. The conduct of a developmental health examination calls for certain types of measurement which are discussed in some detail in the body of this paper.

3. Some of these determinations may readily be incorporated in the routine pediatric serial examinations, especially the determinations of physical growth and maturation which, properly interpreted, throw a very significant light on the progress of growth in childhood.

4. Of these determinations now available the roentgenographic investigation holds the greatest immediate promise.

5. Greater precision in definition of the superior type of childhood is easily attainable as well as in the segregation of simple and self-rectifying types of retardation from the pathological forms which call for medical supervision to restore metabolic integrity.

6. The developmental health examination opens up a new vista of understanding in the problems and personality of the healthily growing child.

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THE MEASUREMENT OF ABERRANT DEVELOPMENTAL GROWTH

I. The Management of Preadolescent Disturbance

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THE SUBTHYROID STATE

ANOMALIES of human stature, proportionate growth and maturity level, more especially gigantism and dwarfism, have always fascinated the investigator. Quite recently, with the accumulating knowledge of ductless glandular physiology, disturbed metabolic states have been carefully studied and numerous theories have been advanced to explain the effects of altered metabolism on the progress and end-result of growth and development.

Recent experience emphasizes the value of skeletal assessment in the diagnosis and treatment of disorders which involve growth in size or progress toward the mature condition. In our laboratory more than two thousand complete human skeletons and more than thirty-six hundred living individuals below the age of twenty-five, studied roentgraphically, have been used to elaborate standards of progress in maturation. Todd[1, 2, 3, 4] and Stevenson[5] have reported this work. These standards have been utilized in the assessments to follow since they have been worked out and tested more fully than other devices of similar nature. It is possible by this method to estimate the stage of ossific development within a six-month range.

In the study and treatment of aberrant growth it is important to evaluate the anomalous progress toward maturity in the individual. Indeed it is in this aspect of developmental growth that the first evidence of a disturbed metabolism is to be found. Engelbach and McMahon[6] and Shelton[7] have recently emphasized the retarding effect of hypothyroidism. The current tendency, however, to speak of maturation solely in terms of sexual maturity does not adequately interpret the maturation process. Differentiation of features indicates, as clearly as growth in stature, a constant structural change just as significant in its assessment before adolescence as at that precise phase of life. The W. R. U. standards evaluate these structural changes throughout childhood and adolescence and are proving valuable in the understanding of all types of failure in the attainment of average developmental progress. In the first volume of the White

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House Conference reports on Growth and Development[8] some of the conditions which lead to a severe lag in maturation are discussed. Diabetes, for example, as well as hypothyroidism and other altered metabolic conditions, handicaps the growing child in that it retards his progress toward maturity as well as the attainment of his average family stature.

INDIRECT DEVELOPMENTAL GROWTH PROMOTION

In these special cases we have studied both retardation in growth and retardation in development, using, for this purpose, anthropometric, clinical, developmental, and psychometric technics, and bringing each

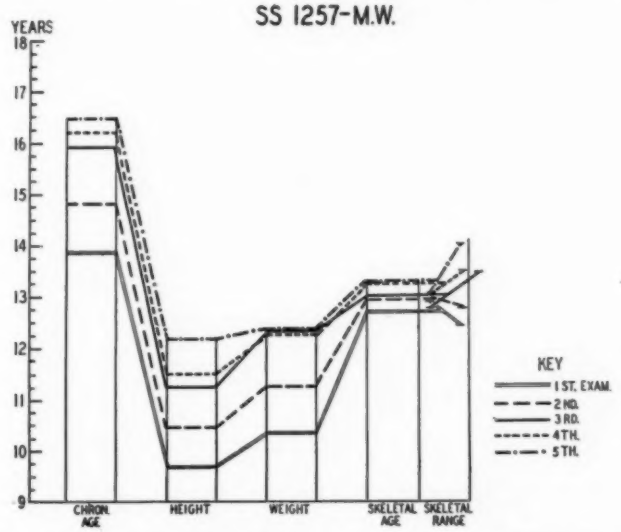

Fig. 1.—Chart of growth and maturation progress of SS 1257, male, white, from the age of thirteen years ten months to sixteen years five months. Treatment only after third examination at fifteen years eleven months. In skeletal range downwardly directed lines signify retardation; upwardly directed lines, progressive maturation.

patient into the laboratory at three-month intervals for study while under active treatment. Nearly 200 cases of disturbed development have been recorded and more than 35 cases are being studied and treated at the present time. We have observed that when a nutritional disorder occurs in a growing child, there is a disturbance of developmental growth. In the majority of children this interruption is temporary and the normal progress is again resumed during the period of convalescence. In a few children, following such a disturbance, there is no resumption of the original tempo of progress, as though the mechanisms which control growth and development had been definitely mutilated. In these cases a progressive developmental lag be-

comes apparent and adult proportions or complete maturity may never be reached. A dwarfism or at best a defective maturation results.

In the treatment of these conditions the administration of certain endocrine substances appears to rectify the metabolic functions of the organism and thus promote developmental growth. It is, however, essential to govern the dose by a serial study of developmental growth progress during the treatment. The following cases illustrate how progress under therapy is studied and indicate the promotion of growth at a rate greater than that shown in normal children under our observation or in cases of aberrant growth not under treatment.

SS 1257 shows a lag both in stature increment and in maturation, with the progress in stature following growth promotion. (Fig. 1,

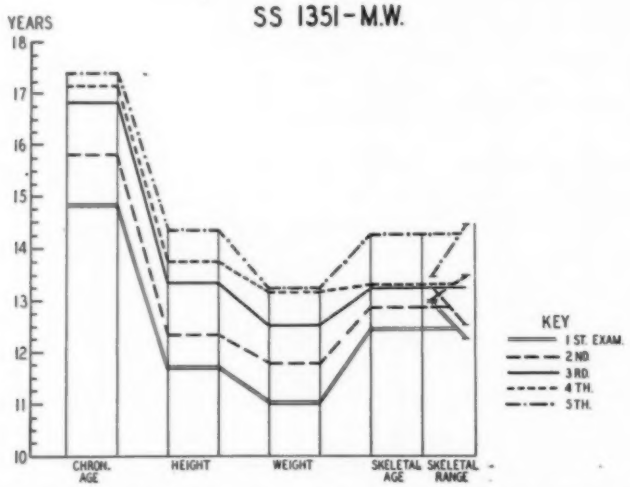

Fig. 2.—Chart of growth and maturation progress of SS 1351, male, white, from the age of fourteen years ten months to seventeen years four months. Treatment only after fourth examination at seventeen years one month. In skeletal range downwardly directed lines signify retardation; upwardly directed lines, progressive maturation.

Table I.) During the first two years while the boy was being studied but not treated, height, weight, and maturation showed much less than the average yearly increments, so that on his sixteenth birthday the boy was retarded the equivalent of four years eight months in height, three years seven months in weight on the Baldwin-Wood standards, and two years nine months in maturation on W.R.U. standards. During the next six months Armour's desiccated thyroid (4 grains) and Armour's desiccated anterior pituitary (2 grains) were administered daily by mouth. Assessments then registered a height increase equivalent to eleven months on the Baldwin-Wood standards, a stationary weight, and a maturation (or developmental) increment

TABLE I

SS 1257

EXAM.	CHRON. AGE	HEIGHT (MM.)	HEIGHT-EQUIVALENT (BALDWIN-WOOD)	WEIGHT (POUNDS)	WEIGHT-EQUIVALENT (BALDWIN-WOOD)	SKEL. AGE (TODD)	SKEL. RANGE (TODD)
1.	13 yr. 10 mo. 9 days	1353	9 yr 8 mo.	74¼	10 yr. 4 mo.	12 yr. 8 mo.	12 yr. 5 mo. to 12 yr. 11 mo.
2.	14 yr. 9 mo. 26 days	1389	10 yr. 5 mo.	79	11 yr. 3 mo.	12 yr. 11 mo.	12 yr. 9 mo. to 13 yr. 0 mo.
3.	15 yr. 11 mo. 9 days	1433	11 yr. 3 mo.	87¼	12 yr. 4 mo.	13 yr. 0 mo.	12 yr. 9 mo. to 13 yr. 5 mo.
4.	16 yr. 2 mo. 11 days	1446	11 yr. 6 mo.	86	12 yr. 3 mo.	13 yr. 3 mo.	13 yr. 0 mo. to 13 yr. 5 mo.
5.	16 yr. 5 mo. 13 days	1470	12 yr. 2 mo.	86¾	12 yr. 4 mo.	13 yr. 3 mo.	13 yr. 0 mo. to 14 yr. 0 mo.

During two years without treatment the increases are:

Height equivalent	19 mo.
Weight equivalent	24 mo.
Skel. age	4 mo.

After six months' treatment the increases are:

Height equivalent	11 mo.
Weight equivalent	0 mo.
Skel. age	3 mo.

TABLE II

SS 1351

EXAM.	CHRON. AGE	HEIGHT (MM.)	HEIGHT-EQUIVALENT (BALDWIN-WOOD)	WEIGHT (POUNDS)	WEIGHT-EQUIVALENT (BALDWIN-WOOD)	SKEL. AGE (TODD)	SKEL. RANGE (TODD)
1.	14 yr. 10 mo. 0 days	1447	11 yr. 8 mo.	77¾	11 yr. 0 mo.	12 yr. 9 mo.	12 yr. 3 mo. to 12 yr. 11 mo.
2.	15 yr. 9 mo. 26 days	1484	12 yr. 3 mo.	82½	11 yr. 9 mo.	12 yr. 10 mo.	12 yr. 9 mo. to 13 yr. 0 mo.
3.	16 yr. 10 mo. 2 days	1537	13 yr. 4 mo.	88½	12 yr. 6 mo.	13 yr. 3 mo.	12 yr. 11 mo. to 13 yr. 5 mo.
4.	17 yr. 1 mo. 24 days	1570	13 yr. 9 mo.	95¼	13 yr. 2 mo.	13 yr. 3 mo.	13 yr. 0 mo. to 13 yr. 5 mo.
5.	17 yr. 4 mo. 21 days	1600	14 yr. 4 mo.	96¾	13 yr. 3 mo.	14 yr. 3 mo.	13 yr. 5 mo. to 14 yr. 5 mo.

During two years without treatment the increases are:

Height equivalent	18 mo.
Weight equivalent	18 mo.
Skel. age	6 mo.

After six months' treatment the increases are:

Height equivalent	12 mo.
Weight equivalent	9 mo.
Skel. age	12 mo.

equivalent to three months on the W.R.U. standards. This case is recorded merely as an example of the encouragement of stature increase in retarded adolescence.

SS 1351 is a similar case in which the developmental progress was materially modified following treatment (Fig. 2, Table II).

After two years of simple observation, when this boy was sixteen years ten months of age he was still retarded the equivalent of three years six months in height, four years four months in weight on the Baldwin-Wood standards, and three years seven months in development on the W.R.U. standards. Further, the retardation was progressive during the two preceding years when no treatment was given. In

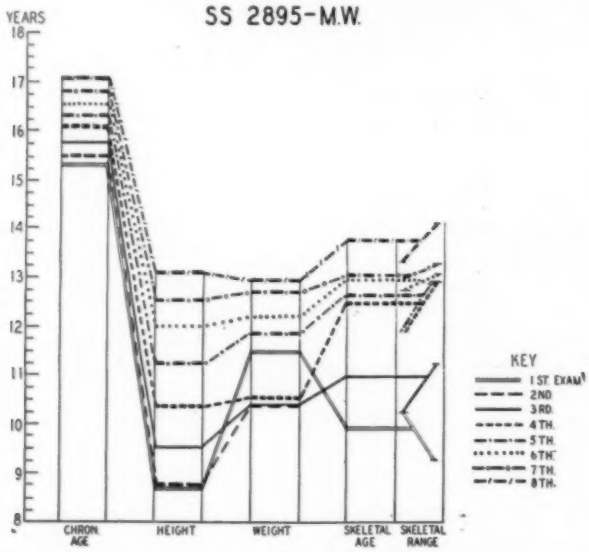

Fig. 3.—Chart of growth and maturation progress of SS 2895, male, white, from the age of fifteen years four months to seventeen years. Treatment throughout entire eight examinations. In skeletal range downwardly directed lines signify retardation; upwardly directed lines, progressive maturation.

the six months following the institution of treatment the patient grew the equivalent of twelve months in height and nine months in weight. He also progressed the equivalent of twelve months in development. During this time he received 2 grains of desiccated thyroid and 2 grains of desiccated anterior pituitary for three months, then 4 grains of each for three months. This is again an illustration of developmental growth encouragement in retarded adolescence.

The detailed relationship of endocrine dosage to progress in developmental growth is presented in the following case (SS 2895), the features of which clearly indicate that a therapeutic program for the promotion of specific effect either of increase in dimensions or of pro-

TABLE III

SS 2895

EXAM.	CHRON. AGE	HEIGHT (MM.)	HEIGHT-EQUIVALENT (BALDWIN-WOOD)	WEIGHT (POUNDS)	WEIGHT-EQUIVALENT (BALDWIN-WOOD)	SKEL. AGE (TODD)	SKEL. RANGE (TODD)
1.	15 yr. 4 mo. 13 days	1310	8 yr. 8 mo.	84½	11 yr. 6 mo.	9 yr. 11 mo.	9 yr. 3 mo. to 10 yr. 3 mo.
2.	15 yr. 6 mo. 6 days	1312	8 yr. 8 mo.	74½	10 yr. 4 mo.	(No roentgenograms made)	
3.	15 yr. 9 mo. 7 days	1347	9 yr. 6 mo.	74¾	10 yr. 4 mo.	10 yr. 11 mo.	10 yr. 3 mo. to 11 yr. 3 mo.
4.	16 yr. 0 mo. 13 days	1387	10 yr. 4 mo.	75¾	10 yr. 6 mo.	12 yr. 5 mo.	11 yr. 9 mo. to 12 yr. 11 mo.
5.	16 yr. 3 mo. 20 days	1426	11 yr. 2 mo.	83	11 yr. 10 mo.	12 yr. 7 mo.	11 yr. 9 mo. to 12 yr. 11 mo.
6.	16 yr. 6 mo. 20 days	1462	12 yr. 0 mo.	85½	12 yr. 2 mo.	12 yr. 11 mo.	12 yr. 9 mo. to 13 yr. 0 mo.
7.	16 yr. 9 mo. 19 days	1492	12 yr. 6 mo.	89	12 yr. 8 mo.	13 yr. 0 mo.	12 yr. 11 mo. to 13 yr. 3 mo.
8.	17 yr. 0 mo. 18 days	1522	13 yr. 1 mo.	92¼	12 yr. 11 mo.	13 yr. 9 mo.	13 yr. 3 mo. to 14 yr. 0 mo.

After twenty months' treatment the increases are:

Height	212 mm. (8⅓ in.)	Height equivalent	4 yr. 5 mo.
Weight	6.75 lb.	Weight equivalent	1 yr. 5 mo.
Skel. age	3 yr. 10 mo.		

gressive maturation can indeed be worked out. This case particularly illustrates the adjustment of endocrine dosage for the promotion of growth and emphasizes the significance of a serial maturation study. (Fig. 3, Table III.)

SS 2895 was first studied in this laboratory on May 9, 1931. The boy had been a feeding problem during the first two years of his life, after which time he failed to grow normally. At the age of four he had measles, at five chickenpox and at six

A *B*

Fig. 4.—*A*. Roentgenogram of left hand SS 2895 before treatment, aged fifteen years four months. *B*. Roentgenogram of left hand SS 2895 after twenty months' treatment, aged seventeen years.

mumps. Other than this his history was uneventful. His parents are both above the average stature and his family history is negative.

In 1926 he had a course of both thyroid and anterior pituitary substance by mouth and became so nervous that after two months treatment was discontinued. In 1928 he had another course of thyroid treatment but this was also discontinued because of nervousness and irritability.

When first examined in our laboratory he was a fairly well-proportioned boy, somewhat lethargic, fifteen years four months thirteen days of age. His voice

had not changed. There was no axillary, pubic, or facial hair. The skin and hair were very dry and the subcutaneous tissues were unusually firm. The genitalia were underdeveloped: testicles about one and one-half centimeters in diameter and penis four centimeters in length. There was also an underdevelopment of the maxillary part of the face with an associated constriction of the posterior nasal passages. The basal metabolic rate registered minus 19 per cent and minus 17 per cent on two estimations. Other laboratory chemical tests revealed nothing unusual.

The physical assessment at this time (Exam. 1, Table III) gave the boy a height age of eight years eight months, weight age of eleven years six months on the Baldwin-Wood standards, and a skeletal age of nine years eleven months on our

Fig. 5.—*A*. Roentgenogram of left knee before treatment SS 2895, fifteen years four months. *B*. Roentgenogram of left knee after treatment SS 2895, seventeen years. Note transformation of cauliflower-like mineralization of patella into normal ossification after twenty months.

standards. There was a marked osteochondritis of the patella and of the navicular bone of the foot.

At this time Armour's thyroid gland tablets were prescribed, 2 grains each day, and Armour's anterior lobe pituitary tablets, 4 grains a day. Two weeks later the dose was increased to thyroid, 4 grains, and pituitary, 6 grains. This dosage produced headache, sleeplessness, and a mild glycosuria. It was therefore reduced to 2 grains of thyroid and 6 grains of pituitary a day. Two weeks later the glycosuria and other disturbances had disappeared and the 4-grain thyroid, 6-grain pituitary dosage was resumed. No further disturbances occurred.

After two months of this régime (Exam. 2, Table III) the boy had lost ten pounds in weight and had not increased in height. The skin was then not so dry and the subcutaneous tissues had lost their unhealthy firmness.

After five months on this dosage (Exam. 3, Table III) it was found that the skin and hair had become quite normal in appearance. The height had increased the value of ten months and skeletal development twelve months. Weight on the other hand showed no change since the previous examination (Exam. 2).

The dosage was now increased to 8 grains of thyroid and 8 grains of anterior pituitary substance a day. Three months later (Exam. 4, Table III) the height had increased the equivalent of an additional ten months, weight two months, and skeletal development eighteen months. There was a beginning of the sexual development and a nearly complete healing of the osteochondritis originally noted.

In view of the greater progress in physical development over height increase the pituitary medication was stopped and the thyroid decreased to 2 grains a day. After another three-month interval (Exam. 5, Table III) it was found that the height had increased the value of ten months and weight sixteen months but skeletal development had remained practically stationary. There was an unhealthy firmness of the subcutaneous tissues as when the boy was first seen and his skin was quite dry. The genitalia, however, had begun to increase in size and there was now a scant amount of pubic hair. Because of the reappearing hypothyroidism the dosage of thyroid was raised to 4 grains a day and the pituitary substance again started at 2 grains a day.

After three months on this dosage (Exam. 6, Table III) the height had progressed the value of ten months and the weight four months. The skeletal development had also progressed the value of four months. The dosage was continued and after another interval of three months (Exam. 7, Table III) the height had progressed the equivalent of an additional six months and weight six months, but skeletal development now remained almost stationary.

At this time it was noted that there was a mild osteoporosis developing in the texture of the bones, particularly in the hands. Consequently vitamins A, B (with G), and D were prescribed and calcium lactate was given in a dosage of 10 grains a day; the thyroid dosage was raised to 6 grains a day and pituitary to 3 grains a day. A month later the boy had a moderately severe attack of influenza during which time the endocrine preparations were discontinued for three weeks and then resumed.

At the next examination (Exam. 8, Table III) height had progressed the equivalent of seven months, weight three months and maturation nine months. By this date the osteoporosis had again disappeared.

Thus, in twenty months weight had progressed 7¾ pounds, the value of one year five months (i.e., eleven years six months to twelve years eleven months); height 212 mm. (8⅓ in.) the equivalent of four years five months (eight years eight months to thirteen years one month); and skeletal development the equivalent of three years ten months (nine years eleven months to thirteen years nine months).

The change in the skeletal age is well shown by the penetration of bone into the epiphyseal cartilages of the left hand (Fig. 4-*A*, *B*). The evaluation of the former is nine years three months whereas that of the latter is thirteen years. (For the criteria of evaluation see Reference 3.)

The transformation of cauliflower-like mineralization of the patella into a healthy ossification during this period of treatment is evident in Fig. 5 which shows the left knee at fifteen years four months and at seventeen years respectively.

SUMMARY

1. Serial examinations in growth studies of children should include assessments of physical maturation as well as of physical growth.

2. In the cases here reported, the W.R.U. standards of physical maturation, assessed on roentgenograms of the skeleton, are employed be-

cause they permit greater precision of assessment than the standards put forward by other workers.

3. Illustrative instances from our studies of aberrant growth are here presented to demonstrate the tempo of progress before and during treatment for developmental growth promotion.

4. Two boys are chosen from our series of retarded adolescence. Their progress in developmental growth for two years preceding active intervention is presented and with this is presented their progress during six months of endocrine treatment devised to hasten an adolescence already considerably delayed. It is not intended to suggest that, lacking treatment, these boys would not ultimately have matured but it is contended that developmental growth metabolism has been favored and stature probably increased by treatment.

5. A third case is presented in some detail to illustrate how adjustment of dosage and proper care in the utilization of extracts from the different endocrine glands permit one to promote increase of stature or progressive maturation as serial assessment of the case may require. The case chosen (SS 2895) is a relatively simple form of retarded developmental growth in which thyroid and pituitary substances were adequate to promote satisfactory results since the deficiency was uncomplicated by actual defects due to chronic disturbance of growth, to long continued focal infection, or other constitutional mutilation. It must not be assumed that every case treated will resolve so readily or display so marked a sensitivity to modifications in the régime of treatment as is so beautifully demonstrated in SS 2895.

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A SURVEY OF ONE HUNDRED CASES OF CONGENITAL SYPHILIS TREATED WITH STOVARSOL (ACETARSONE)

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DURING the past few years the use of stovarsol (acetarsone*) in the treatment of syphilis, especially congenital syphilis, has been detailed by a number of writers.[1-8] A survey of 100 cases of congenital syphilis thus treated seems desirable at this time. Our treatment was patterned after that of Bratusch-Marrain, which is as follows: 0.005 grams of the drug per kilo body weight is given for one week, followed by 0.010 grams per kilo daily for one week, 0.015 grams per kilo daily for one week, and 0.020 grams per kilo daily for six weeks. This is followed by a rest period of one month and the course repeated until the serologic tests are entirely negative, and three courses are given thereafter. A rest period of six months is then given and then one more course of treatment.

The serologic tests used by us consist of a Wassermann reaction, using acetone insoluble and cholesterinized antigens, and a Kahn test. In our series there were 46 cases in which treatment was begun in the first year, and 54 cases in which treatment was started in children over one year of age. This division is made because treatment in the young infant results, as a rule, in prompter clinical and serologic improvement.

TOXIC REACTIONS

Toxic reactions occurred three times in the older group and twice in the younger group. In this latter group there were 3 patients who developed toxic reactions in whom it was doubtful that the symptoms were due to stovarsol. Thus the percentage for the series showing toxic reactions was 5 and possibly 8. Most of these reactions were very mild, consisting of an erythema and in a few cases a rise of temperature. Diarrhea did not appear as a toxic symptom in our series of cases; when it was present it was due to some other cause. In one patient a girl of ten and a half years, there was a marked erythema when given sulpharsphenamine, but no reaction to stovarsol.

Three patients in the older group showed toxic reactions. One was a boy, three years five months old, who developed a generalized macular rash twelve days after beginning treatment. Stovarsol was dis-

From the syphilis clinic of the Childrens Memorial Hospital, Chicago, Ill.

*Acetarsone is the name used in "New and Non-official Remedies" of the American Medical Association and is the same chemically as stovarsol and spirocid. The drug, stovarsol, used in this series was kindly furnished to us by Merck & Co.

continued for two weeks and then resumed without reaction. The second patient, a girl, five years nine months old, developed an erythema on the dorsal surfaces of the upper and lower extremities a few days after treatment was begun. No treatment was given for a week. The rash disappeared and treatment with stovarsol was begun again, this time without reaction. The third patient, a white girl of seven years, had an interstitial keratitis. After three weeks of treatment she developed an erythema over the upper chest and the dorsal surfaces of the upper and lower extremities together with fever up to 102.5° F. Stovarsol was discontinued and begun in ten days when a similar cutaneous and febrile reaction occurred. Stovarsol was not attempted again. During this time, however, the keratitis made very rapid improvement, the right eye almost clearing, and the left cornea remaining only slightly hazy.

Two patients in the group treated during the first year showed toxic reactions. One was a white girl of nine months who, on the day after the beginning of stovarsol treatment, developed a temperature of 104° F. There were no associated findings and the temperature returned to normal the next day. On the day following the day of normal temperature, through a misunderstanding, the mother gave another dose of stovarsol and this time the temperature rose to 103° F. Gray powder was then given for two weeks, after which stovarsol was again given and this time without reaction. The other patient in this group was a white boy two months old who was given 0.05 gm. of stovarsol for two days. He developed a temperature of 104° F., and had a convulsion as reported by the neighborhood physician who cared for him and subsequently treated the syphilitic condition.

In three patients of this younger group it was doubtful that the patient reacted adversely to stovarsol. The first patient was a congenital syphilitic admitted to the hospital with bronchopneumonia, bilateral purulent otitis media, large spleen and liver, and bone syphilis. Three days after treatment with 0.06 gm. of stovarsol daily he died. The second was a white infant of three months with bronchopneumonia, visceral and mucous membrane syphilis, who was given 0.06 gm. of stovarsol daily for three days. Antisyphilitic medication was discontinued because he seemed very sick. He died three days later. There was no evidence that death was connected with stovarsol. The third patient in whom stovarsol had a doubtful toxic effect was a girl of six weeks with a bloody discharge dripping from her nose. The head was held retracted. There were scaling and infiltration of the intereyebrow region, a maculopapular rash, cylindrical-shaped chest and abdomen, with marked retraction of the lower chest with each inspiration; the liver was firm and on a level with the umbilicus. The patient died after 0.06 gm. of stovarsol had been given for two days.

SEROLOGIC REACTIONS

Serologic response was very satisfactory. For purposes of comparison to the stovarsol treatment, we treated a group of 29 infants, beginning in the first year and continuing for one year, by the older methods of treatment; that is, with injections of mercury, bismuth, and the arsenicals, and gray powder by mouth. The same was done with a group of 48 patients in whom treatment was started after the first year of age and continued for one year. In the younger age group of 46 cases there were 35 treated with stovarsol for one year. Of this group 3, or 8 per cent, were positive at the end of one year of treatment. One in this group of 35 had negative serologic tests when first seen at seven weeks. Treatment was given to the child, however, because the mother had syphilis with very little prenatal treatment, and the child was pale, had snuffles and a palpable spleen. This leaves 3 out of 34 cases or about 9 per cent still positive. In 20 of these cases in which treatment was begun in the first year, reversal followed the first course of treatment; in 7 it followed the second course, and in 4 it followed the third course.

In this age group of the 29 cases previously mentioned, treated by the older methods of treatment, 18 or 62 per cent were positive after one year of treatment. These must not be considered Wassermann-fast cases, as many of them became negative in the second, third, or fourth years of treatment, and the same applies in the older age groups.

In the older age group of our series of 54 cases treated with stovarsol, 23 were not treated for as long as a year, leaving 31 cases. Three of the 31 cases, however, had negative serologic tests on the blood when treatment was begun; one of these three had a positive spinal fluid. Of the remaining 28 cases treated for one year, 16, or about 57 per cent, showed reversal following treatment, as compared to 80 per cent positive, or about 20 per cent, which showed reversal at the end of one year of a group of 48 cases treated by the older methods. As stated, these must not be considered Wassermann-fast, as many later became negative. In this older group a few had some little treatment before stovarsol was begun.

In this group of 28 older children treated with stovarsol, 5 patients became negative following the first course, 5 following the second, and 6 following the third course. By reversal we mean not only an entirely negative Wassermann test but also a negative Kahn test. Frequently the Kahn test was persistently one- or two-plus when the Wassermann was negative.

The patient with the positive spinal fluid and the negative blood tests is of sufficient interest to be detailed here. R. T., at about three and a half years of age, developed attacks of unconsciousness lasting fifteen to twenty minutes. These were two to three weeks apart. He had been treated in a neuropsychiatric clinic with

calcium lactate, gr. x, t.i.d. which seemed to free him of these convulsive attacks. However, he began to have severe spells of night crying which could not be explained by the parents. They were so prolonged that on several occasions the neighbors threatened to call the police. He was so irritable, quarrelsome, and constantly on the go, that he could hardly be managed at the near-by settlement house. He behaved in a similar manner at the dispensary. After several months it was learned that the parents had syphilis and were under treatment. The child was sent to us for a consideration of syphilis. We found a boy of four years and four months, with a squarish head, with marked veins and prominent frontal bosses, and suggestions of rhagades about the mouth. As stated the blood Wassermann and Kahn tests were negative but the spinal fluid Wassermann was acetone insoluble antigen one-plus, cholesterinized antigen two-plus. The Lange colloidal gold test and the Pandy test were negative. The cell count was 15, mostly lymphocytes.

Treatment with stovarsol was begun and in a month the mother, unsolicited, reported that he was sleeping better and that he was much more easily managed. At the dispensary the child was tractable and quiet. Because we were dealing with cerebrospinal syphilis our dosage was increased to one-fourth more than our usual full dose. After six months of treatment the spinal fluid was entirely negative and now after a year his general condition and behavior are excellent.

In one patient in the younger group treatment was begun at nine months of age. The general improvement was excellent but the Wassermann seems fast. That Wassermann-fast cases occur also with the older type of treatment and even when treatment is begun very early is shown in the following case.

A boy three weeks old had mercury injections with alternate courses of sulpharsphenamine in full doses and gray powder by mouth for fourteen months. At the end of this time he had four-plus Wassermann and Kahn tests. The family was dissatisfied because the serologic tests were not negative and took the child to a clinic where bismuth therapy was given. After a year they returned because the serologic tests were still four-plus.

Improvement in the general condition of these patients is the rule. Their color improves rapidly and many gain markedly in weight. For example, one child of two and one-half years gained 7 pounds in eight months; another, a girl of seven years three months, who weighed 35 pounds when treatment was begun, gained 7 pounds in four months without change in régime. Condylomata disappeared in from one to two weeks. Interstitial keratitis responded more rapidly than usual; e.g., the first case detailed in the older children with toxic symptoms. Another was able to read two lines farther down on the chart for testing vision after four weeks of treatment. James[8] reports 7 cases of interstitial keratitis in which very satisfactory improvement was made with stovarsol. Hydrarthrosis and bone lesions responded very well. The improvement in one case of cerebrospinal syphilis is recorded.

SUMMARY

One hundred cases of congenital syphilis treated with stovarsol are surveyed. Serologic and clinical improvement was very good. Toxic

reactions to the drug occurred in from 5 to perhaps 8 per cent of the cases, and they were usually mild in character. Serologic reversal was very much better with stovarsol than with the older methods of treatment.

CONCLUSION

Stovarsol by mouth in rational conservative dosage, such as that of Bratusch-Marrain, is a valuable drug in the treatment of congenital syphilis.

4753 BROADWAY.

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CONGENITAL OSTEOSCLEROSIS

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CONSIDERABLE interest has been aroused in the study of bone changes in anemia as a result of the reports of Cooley, Witwer and Lee,[1] Vogt and Diamond[2] and others. In the condition described by these authors, there is a widespread bone change which apparently develops secondarily to a peculiar type of anemia. In the condition to be reported in this paper, an anemia is found associated with bone changes, but the relationship of cause and effect seems to be altered.

Albers-Schönberg,[3] whose name usually identifies this disease, first called attention to the condition in 1904. Since that time, less than 40 cases have been described under a variety of different names. These include marble bones, osteosclerosis congenita, osteosclerosis fragilis generalisata, osteosclerotic anemia, osteosclerosis with various types of leucemia and osteopetrosis. Karshner[4] has reviewed the literature to 1926 and gives abstracts of all cases reported together with a description of the clinical course and the roentgenologic findings. Pririe[5] has, more recently, described the progress of the disease as revealed by the roentgenogram in a series of cases which he has been able to follow over a period of twenty-one months.

The characteristic finding in congenital osteosclerosis is the roentgenologic demonstration of an overgrowth of the cortical portion of bone at the expense of the medullary cavity. The overgrowth is entirely endostal and no enlargement of the bone occurs except in connection with the ends of the long bones, where clubbing and deformity is frequently found. All bones of the skeleton are involved but the degree of involvement may vary in different parts. When the osteosclerosis is fully developed, the roentgenogram reveals a dense, homogenous bone shadow in which no normal markings or evidence of normal bone structure can be discerned. This appearance is usually most evident in the bodies of the vertebrae, the central portions of the pelvis, the base of the skull and the ends of the long bones. The roentgenogram usually demonstrates striations in the flat bones parallel to the borders and transverse striations or bands of lessened density in the sclerosed areas of the long bones. In these bands, bone trabeculations can be seen, a fact which is taken to indicate the occurrence of remissions in the course of the disease.

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The secondary manifestations of the disorder are the most important. These include retarded growth, anemia with enlargement of the liver, spleen and lymph glands, hydrocephalus, optic atrophy, pathologic fractures, imperfect dentition and mandibular suppuration. The secondary manifestations are not constantly present but vary with the degree of involvement of the bones. The severe forms usually occur in childhood, usually show a fairly complete development of secondary manifestations and are progressively fatal.

The disease exhibits a distinct familial tendency in its incidence. Multiple cases in a single family have been reported by several authors. In four instances the condition has occurred in one of the parents as well as in the child[5, 6, 7, 15] but in most instances the parents have been normal.[8, 9, 10, 11]

It appears as though the disease has its beginning in fetal life. Pririe reports a roentgenogram showing a fetus in utero which, from the density of the vertebrae, suggested a case of marble bones. He reports this child again, at the age of five years, as a definite case of marble bone disease. Three necropsies have been recorded in which osteosclerosis has been found in infants dying soon after birth.[12, 13, 14] The condition is more frequently met with during childhood but has been recorded as late as fifty-eight years of age.[16]

The cause of the disorder is not known. Heredity, congenital osteogenetic defect, syphilis, chronic infection, endocrine disturbance involving any or all of the following glands, hypophysis, parathyroids, thyroid and thymus, and avitaminosis, all have been indicted by different authors as the cause. While the occurrence of the condition in association with endocrine disorders is frequent, heredity or a congenital defect in osteogenesis seems to be a logical interpretation of the etiology.

The pathogenesis of the condition is not understood. It would seem as though there must be an alteration in the calcium and phosphorus metabolism but, save for a few determinations, the blood chemical values for calcium and phosphorus have been found to be normal. Determinations of calcium balance have revealed an increased urinary excretion of calcium but no definite evidence of increased retention.[17] The calcium content of the pathologic bone has been found to fall within normal limits. Kooylow and Runowa[18] have shown a marked decrease in the phosphorus and an increase in the magnesium content of the pathologic bone.

As a part of the general retardation of growth, the development of centers of ossification is usually delayed and ossification of the cranial sutures is late. The interference with growth has been explained on the basis of dysfunction of the hypophysis. The osteosclerotic process in the skull produces marked changes in and about

the sella turcica. Frequently the sella is narrowed and a characteristic finding is thickening and clubbing of the posterior clinoid process. At necropsy the hypophysis is usually small.

The type of anemia found in these cases is not specific. It is brought about in the replacement of bone marrow by cortical overgrowth and does not differ from anemia produced by the replacement of bone marrow by tumor metastases or leucemic infiltrations. This type of anemia is usually termed osteosclerotic or myelophthisic anemia.[19, 20] The characteristics of this anemia are as follows: There is a marked reduction in both the erythrocyte count and the hemoglobin content, making the color index slightly under 1. Anisocytosis and poikilocytosis are present and immature, nucleated red cells are usually found. Myelocytes and myeloblasts are present in the blood smear. The increase in the myeloid cells may bring about a leucocytosis though a leucopenia is not unusual. As a terminal manifestation, there may be a decrease in blood platelets and other characteristics of aplastic anemia. The severity of the anemia is dependent on the amount of bone marrow destroyed by cortical overgrowth but is influenced by the regenerative power of the remaining marrow and the degree of extramedullary hematopoiesis which may occur.[21]

Enlargement of the liver, spleen and lymph glands is a common finding associated with anemia. Pathologically these organs show a marked myeloid reaction with extramedullary hematopoiesis which might be considered a reversion to the embryonic type of blood formation. In one necropsy foci of hematopoiesis were found in the kidney.[16] The degree of metaplasia of the myelogenous elements may result in the production of a blood picture which resembles that of leucemia.

Bone changes occurring in the skull, while not limited to the base, are most marked in this area. The most remarkable point in connection with the sclerosis of the base of the skull is the narrowing of the foramina which is produced. Hydrocephalus has been noted, particularly in the younger patients, and has been explained as arising from the circulatory disturbances produced by the narrowed foramina. A more important result of the changes at the bast of the skull is the production of optic atrophy. Like hydrocephalus, optic atrophy is noted particularly in the younger cases, but the two phenomena are not always found associated. Optic atrophy is probably produced by pressure on the nerve as it passes through the narrowed optic foramen. Epistaxis may be a manifestation of pressure on the ophthalmic vein. Distortion of the orbital cavity may cause a slight exophthalmos. In many cases a nystagmus has been observed and interpreted as a result of sclerosis of the bony labyrinth.

The occurrence of pathologic fractures has often made possible the diagnosis of mild forms of the disease. The increased fragility which permits these fractures to occur belies the implied hardness in the descriptive term, "marble bones." Pririe feels that the term, "chalky bones," better describes the condition. Karshner prefers the term, "osteopetrosis." Pathologic fractures have been found as early as four months of age, though they are more usual in later childhood and in adult life. A peculiarity of these fractures is that they occur at right angles to the shaft of the long bones, a feature attributed by some authors to decreased elasticity and, by others, to abnormal fragility at the points of the transverse bands of lessened density which the roentgenogram reveals.

As a part of the general disturbance, dentition is usually delayed and the teeth are imperfect. Dental caries is very common. A marked tendency toward the development of suppuration of the lower jaw has been noted. This process is probably a consequence of insufficient blood supply occasioned by pressure on the alveolar artery as it traverses its bony canal in the mandible.

The course of the disease is essentially chronic. The osteosclerotic process, per se, is not incompatible with life. The secondary manifestations constitute the serious menace to life. The severe forms in childhood are invariably fatal, death being due, early, to severe anemia and asthenia, while, later, suppuration of the lower jaw is usually linked with a fatal outcome. Goodall's patient died at ten weeks with a hemoglobin of 22 per cent, while the earliest death in a case in which suppuration of the jaw was present, occurred at five months. If the disease is not severe enough to produce serious secondary manifestations, the process may become arrested and the outlook, then, is fairly good. There is no known method of eradicating or arresting the osteosclerotic process.

There is no treatment which seems to have any effect on the disease. Treatment with a diet in which calcium is restricted seems to be of no value. The use of ammonium chloride has produced no tangible results. Zadek calls attention to the fact that irradiation of the long bones or spleen is contraindicated. Splenectomy, a procedure which also would seem to be contraindicated, has been performed without benefit. Pehu has advised a partial removal of the parathyroid glands. The little we can do is to endeavor to prevent the occurrence of fractures by guarding against trauma, to enforce strict dental hygiene to avoid dental infections, to supply iron salts and blood building preparations to combat the anemia and to avoid those substances which promote calcification.

The following patient presents the typical picture of congenital osteosclerosis.

CASE REPORT

N. Z., female, Italian, aged ten months, was admitted to the hospital on Dec. 24, 1931, with the complaint of failure to gain. Both grandparents on either side had died, from unknown causes, at advanced age. One of the father's brothers had died at five years of age from a disease which had been present from birth, producing deformities of the legs. An accurate history of this illness could not be obtained. The father and mother of the patient were normal. There were no other children and there had been no other pregnancies. In 1923, the father had received treatment for a chancre. His blood Wassermann test had been negative, at that time, and on repeated examinations in intervening years.

Fig. 1.—Facies at 10 months of age.

The child had been born at full term, by a difficult forceps delivery, after a protracted labor. The birth weight was 6¾ pounds. The newborn period was normal.

The infant had been breast fed for one month and was then changed to a modified cows' milk formula. From birth until three months of age, the child had been given 5 drops of viosterol, three times a day. From three months of age until the time of admission to the hospital, she had received 3 teaspoonfuls of 10-D cod liver oil, daily.

The child was able to sit alone at seven months. The first tooth appeared at eight months.

The parents had always noticed that the child was rather pale and that the pallor was increasing. She had never taken her formula well and had gained weight very slowly. About two months before admission, the infant had bled, a little, from the nose over a period of four days. One week later, this was repeated for a day. There had been no bleeding since that time. There had been no vomiting or other gastrointestinal symptoms.

Physical Examination: The patient was a poorly nourished, poorly developed, female infant weighing 15 pounds and 2 ounces. The facies were rather peculiar; there was a marked pallor with a slight yellowish tinge, the expression was apathetic and rather mask-like, the forehead was broad and high and there were prominent frontal eminences, the cutaneous veins were dilated, the eyes were widely separated and prominent but normally shaped, the bridge of the nose was very slightly depressed, the malar eminences were not prominent, the chin was small and receding, the entire face seemed a little puffy and prematurely aged.

The head measured 45 cm. in its largest circumference. There was a peculiar stony consistency to the cranial bones. There were prominent bosses over the parietal bones with a depression along the sagittal suture. The anterior fontanelle

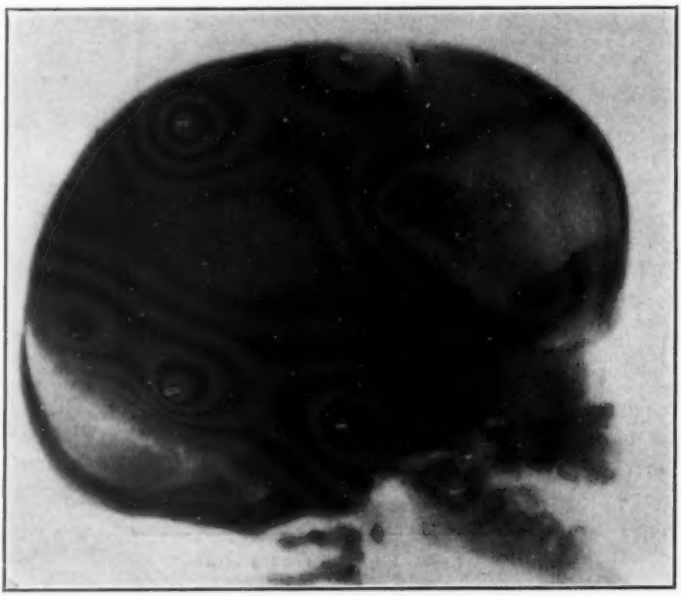

Fig. 2.—Roentgenogram of the skull showing increased density of all cranial bones especially marked at the base. The posterior clinoid process is clubbed.

was open about 2 cm. and was slightly depressed. The bony edges of the fontanelle were firm and slightly everted.

There was a constant, fine, rapid nystagmus. Light perception was apparently present but no other evidence of vision could be elicited. Examination of the fundi showed a bilateral optic atrophy.

There was one tooth present. This had a white, chalky appearance.

The abdomen was full, particularly in the left upper portion. The spleen tip was palpable at the level of the iliac crest, the organ being very firm in consistency and smooth. The liver edge was at the costal margin. The inguinal lymph nodes were slightly enlarged.

There was no deformity of the extremities and there was no disproportion of these parts to the rest of the body.

Laboratory Findings:

Red blood cells	3,480,000	Blood platelets	240,000
White blood cells	7,100	Bleeding time	4 minutes
Hemoglobin	60%	Clotting time	6 minutes
Polymorphonuclears	23%	Normoblasts	8 per 100 W.B.C.
Lymphocytes	49%	Reticulocytes	9%
Mononuclears	15%		
Lymphoblasts	3%		
Myelocytes	7%		
Myeloblasts	3%		

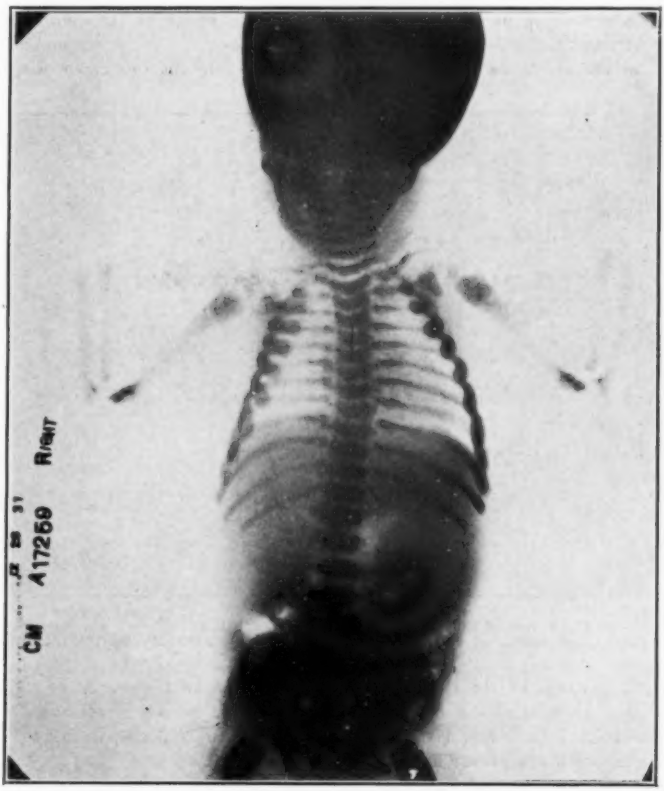

Fig. 3.—All bones of the skeleton showed marked increase in density. In the upper extremity this is most marked at the ends of the bones.

Anisocytosis, poikilocytosis and polychromatophilia present.

Fragility test—hemolysis began at 0.52% and was complete at 0.40% (control —0.44 to 0.32%).

Blood Chemistry—N.P.N.—33.4; Sugar—87.8; Serum Chlorides—596; Calcium—10.1; Phosphorus—4.0; Icterus Index—11; Seroprotein—5.7; Albumin—4.1; Globulin—1.6.

Urinalysis including urobilinogen test was negative.

Blood Wassermann tests on the patient and both parents were negative.

The diagnosis was made by roentgenologic examination. The following report was made by Dr. A. L. L. Bell:

"The skull appears to be of moderate size. The suture lines are normally outlined. All of the bones of the vault and also those of the base are slightly thickened and unusually dense, with a rather marked obliteration of the normal bony architecture and bony trabeculations. The sella turcica is faintly demonstrated and appears to be moderate in size and normal in outline. There is marked increased calcification noted in the clinoid processes which show obliterated bone texture.

"The remainder of the skeleton, including the vertebrae, thorax, upper and lower extremities, and pelvis, all show similar changes. These changes are also noted in the epiphyses. In the long bones, especially in the upper extremities,

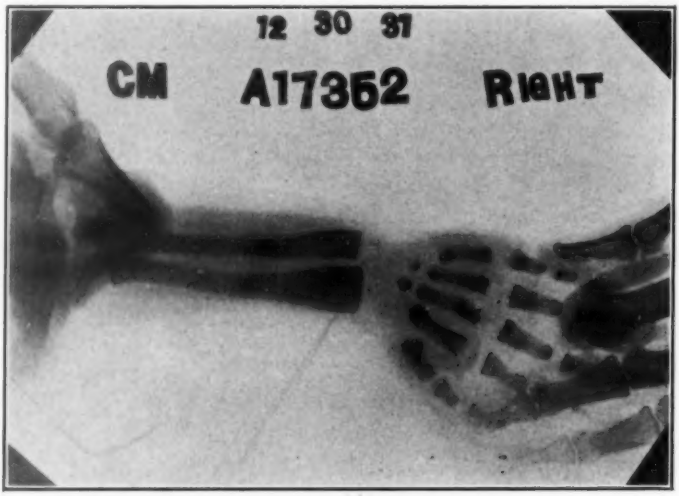

Fig. 4.—In the bones of the forearm transverse striations can be seen near the epiphyses. The bones of the hand show hour-glass areas of increased density.

the mid portions of the shaft show some normal bone trabeculations but in the epiphyseal portions of the shafts on either side there is marked obliteration of the normal bone texture and marked calcification. This is demonstrated to a lesser extent in the bones of the hand."

"Conclusion: 'Marble Bones.'"

The child remained in the hospital for twenty-four days. Two small transfusions were given. Ammonium chloride was given in doses of 5 grams per day. An attempt was made to limit the calcium intake but considerable difficulty was experienced with the administration of solid foods, making it impossible to eliminate milk from the diet. Repeated blood studies showed immature cells in the normoblastic, myeloblastic and lymphoblastic series, with a total white count gradually rising from 7,000 to 15,000. There was a noticeable increase in the size of the spleen and the liver became palpable to 2 cm. below the costal margin. She was discharged from the hospital with a hemoglobin of 70 per cent.

One month later the child was readmitted to the hospital with a hemoglobin reading of 55 per cent, red cell count of 3,160,000 and white cell count of 25,500. There had been little change otherwise in the general condition.

During the year following this, the child was seen infrequently. There was a progressive enlargement of the liver and spleen, a gradual increase in the anemia, poor weight gain, retarded growth and frequent attacks of epistaxis.

The last examination was made at 23 months. About a week prior to this, the child had had a severe epistaxis.

The head measured 46.4 cm. in circumference. The anterior fontanelle was closed and there was a bony bulge in this region. There was a slight exophthalmos. Seven teeth were present, all presenting a flat, chalky, white appearance. The alveolar margins were tremendously thickened so that the arch of the palate was represented by a groove about 1.2 cm. in width and depth. The abdomen measured 55 cm. in circumference. The liver edge was 3.5 cm. below the costal margin. The spleen filled the entire left half of the abdomen, the tip being in the pelvis and the body of the organ producing a bulge in the flank. Epiphyses were slightly enlarged. There were two small purpuric spots on the right leg.

The hemoglobin was 37 per cent; the red cell count, 1,880,000; the white cell count, 49,800; the platelets, 110,000. Bleeding and clotting times were normal. The stained smear presented a most bizarre picture. The differential count was: polymorphonuclears, 29 per cent; myelocytes, 15 per cent; myeloblasts, 10 per cent; lymphocytes, 32 per cent; lymphoblasts, 8 per cent; monocytes, 5 per cent; eosinophiles, 1 per cent; nucleated red cells, 14 per 100 W.B.C.; reticulocytes, 15 per cent. Fragility test—hemolysis began at 0.48 per cent and was complete at 0.32 per cent (control 0.44 per cent to 0.28 per cent). The blood calcium was 9.9 mg. per 100 c.c. and the blood phosphorus was 2.9 mg. per 100 c.c. The icterus index was 8.

Since this examination the chief feature of the child's course has been repeated attacks of severe epistaxis, occurring at weekly intervals but without other purpuric manifestations. In spite of the marked anemia the child recently survived a severe upper respiratory infection.

COMMENT

The striking feature in the history of this case is the large amount of vitamin D which the child received. The idea that osteosclerosis may represent the extreme in the healing of a rachitic process has been advanced but is generally discounted since rachitic changes have not been demonstrated in these cases. The administration of vitamin D may accelerate the progress of the condition. In this connection the blood chemistry is of interest. Both determinations of phosphorus have given low values, the second determination, after thirteen months without added vitamin D in the diet, giving a value suggestive of active rickets. It is difficult to reconcile this last determination with an increased rate of calcium deposition. Though roentgenologic evidence is lacking, it may be that the disease process is in a stage of remission.

The entire subject of the relationship between bone changes and blood changes is probably much more complex than this presentation would seem to indicate. The possibilities that bone changes in this condition are secondary to or simultaneous with bone marrow changes

are refuted by the fact that fairly extensive osteosclerosis has been reported in adults without anemia and with no abnormality in the blood picture.

The blood picture of the anemia of congenital osteosclerosis has many features in common with the blood picture of Cooley's erythroblastic anemia. In both there is a gradually increasing anemia in the face of evidence of intense bone marrow stimulation and regeneration but, in the former, there is increased calcification, and in the latter, decreased calcification. The situation suggests the possibility that the two conditions may be closely related and that osteosclerosis may be secondary to osseous rarefaction. This idea has been frequently advanced but proof is lacking. In this connection a report by Moore[22] is of interest. If my interpretation is correct, in Moore's patient, an adult case of sickle cell anemia, the skull showed the characteristics of the skulls described by Cooley while the short bones showed osteosclerosis. This links three types of anemia and complicates the picture. An analysis would seem to indicate that intense bone marrow stimulation may cause bone rarefaction, that osteosclerosis may follow osseous rarefaction, that osteosclerosis may occur without demonstrable bone marrow changes but that the weight of evidence favors the conception that bone sclerosis or petrifaction in congenital osteosclerosis is the primary condition and that changes affecting the bone marrow and hematopoietic system are secondary.

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8 CLARK STREET.

THE PRODUCTION AND USE OF SOFT CURD MILK

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THE interest of both dairymen and physicians has been recently called to the production of soft curd milk and its adaptation in infant feeding. The term "soft curd milk" is used to designate a milk which, with the addition of rennin forms a softer, flocculent curd, in contrast with the tough curd of ordinary cow's milk. Buckley,[1] and Washburn and Jones[2] in 1916 first reported the fact that milk from certain cows formed such a curd. Espe and Dye[3] in 1930 in their studies on dogs with gastric fistula found that the curd tension of milk affected the persistence but not the rate of gastric secretion. They concluded that curd tension was not the sole factor determining the digestibility of the food. Hill[4] of the Utah Agricultural Experiment described a method for measuring curd tension and advocated the use of soft curd milk unboiled and undiluted, in infant feeding. Elias[5] reported the results of such feeding of 82 infants, varying from birth to 2 years of age for periods from 10 to 90 days. No analyses or descriptions were given of the methods used in the production of the milk which was furnished by the Sheffield Farms Company. Nor were the factors of the age and length of time on the feeding sufficiently considered.

Since both dairy and medical aspects had not been correlated, Dr. K. F. Meyer, Adviser to the California Association of Medical Milk Commissions, suggested that such a closely integrated study be attempted. Accordingly plans were drawn up for the production and analysis of the milk to be made at the Branch of the College of Agriculture at Davis and the clinical application to be made through the Pediatric Department of the University of California Medical School at San Francisco. Frequent meetings and correspondence resulted in a closely supervised study.

PART I. PRODUCTION AND ANALYSIS OF MILK OF LOW CURD TENSION

In preparation for the furnishing of low curd tension milk a survey was made of the cows in the University Farm herd. Those animals which were early enough in lactation to assure their continuing to yield a good supply of milk at the end of a six-month period were desired. It

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was assumed that those animals which produced a milk of low curd tension in the second month of lactation would continue to do so throughout the major part of the remainder of their lactation period. This assumption proved to be erroneous, for it was found that some of those animals, chosen early in March as producers of soft curd milk had changed by April 1 to producers of milk of medium hard curd, necessitating their being discarded. Moreover, throughout the period from April 1 to October it was necessary to replace certain animals with others because of the change in the curd tension of their milk. It was planned to furnish milk of a curd tension below 30 grams, but in reality during certain short periods the tension increased to 30 to 35 grams or even higher on occasion before the individual cow responsible for the increase could be replaced by another of lower tension.

The cows chosen were healthy, nonreactors to tuberculin and abortion tests, and were included in the two-time string. It was planned to furnish the mixed milk of not less than three animals. In all, nine animals were used—6 Holstein-Friesian and 3 Ayrshires. To insure a milk of good quality both from the standpoint of bacterial content and of flavor, not only were the utmost precautions taken from the sanitary standpoint but also feed was withheld from the animals during the five-hour period previous to milking. That the count for the total period showed a maximum of 11,000 per c.c., a minimum of 1,000, and an average of 5,100, and that the milk was of excellent flavor at all times, bespeaks the care of handling and producing.

The milking was done in mid-afternoon; the supply was immediately cooled, bottled, packed in iced containers, and shipped immediately to its destination in San Francisco. One man was responsible for this phase of the study throughout the period. Samples were analyzed chemically daily, were scored for flavor daily, and were examined for bacterial count at least weekly.

Table I summarizes by months the results of the daily chemical analyses. Fat percentages were obtained by the Babcock method, and total solids gravimetrically using the Mojonnier machine, the solids not fat being determined by difference. Casein and total protein were determined using the formaldehyde titration method. It was felt that this method was sufficiently accurate for the routine daily analyses, especially where comparative values were desired. In the determination of ash the standard procedure was employed.

The sole purpose of determining the coagulability by rennin and the P_H value of the milk was to indicate that it was normal milk. Physiological disturbances in the cow have been found to be reflected in these values as definitely as such indices as changes in body temperature, for instance. The rennin coagulation values were determined using a 2 per cent concentration of rennin and temperature of 39.5° C. The P_H values were determined electrometrically using the Type K Leeds and Northrop Potentiometer and Bailey type hydrogen electrode. The rennin coagulation and P_H values clearly indicate that the milks used throughout the study were normal for cow's milk.

The curd tension values were determined using a modification of the method described by Hill.[3] The curd knives were exactly 2 inches in diameter, a Chatillon's improved spring balance was used to measure the tension, but instead of using the

TABLE I

MONTHLY SUMMARY OF THE ANALYSES OF DAILY SAMPLES OF LOW CURD TENSION MILK[1]

DATE		CURD TENSION GRAMS	FAT PER CENT	SOLIDS NOT FAT PER CENT	TOTAL SOLIDS PER CENT	CASEIN PER CENT	PROTEIN PER CENT	ENERGY CALORIES PER KG.	ASH PER CENT	RENNIN COAGULATION TIME	P_H
APRIL	Max.	40	3.89	8.40	11.89	2.45	2.95	690*		5′ 42″	6.69
	Min.	20	3.17	7.48	10.94	2.09	2.52	617		4′ 48″	6.63
	Ave.	32	3.46	7.90	11.35	2.25	2.72	646		5′ 20″	6.66
Reported analyses†			3.4-3.59	9.00	12.46		3.25	690			
MAY	Max.	28	4.15	8.23	12.13	2.21	2.63	708	0.716	5′ 56″	6.75
	Min.	15	3.0	7.65	10.85	1.95	2.25	606	0.695	3′ 20″	6.72
	Ave.	22	3.57	7.90	11.47	2.06	2.49	657	0.706	5′ 00″	6.73
Reported analyses			3.4-3.59	9.00	12.46		3.25	690			
JUNE	Max.	33	4.40	8.44	12.47	2.29	2.76	718	0.716	4′ 30″	
	Min.	15	2.90	7.86	11.07	1.98	2.43	605	0.705	4′ 28″	
	Ave.	25	3.72	8.10	11.79	2.14	2.58	676	0.709	4′ 29″	6.61
Reported analyses			3.72	8.96	12.68		3.31	716			
JULY	Max.	35	4.80	9.10	12.89	2.44	2.94	795	0.722		
	Min.	24	3.50	7.48	10.89	2.20	2.65	632	0.671		
	Ave.	29	3.96	8.21	12.13	2.31	2.78	709	0.697		
Reported analyses			3.90	9.10	13.00		3.27	734			
AUG.	Max.	51	4.60	9.02	13.39	2.57	3.09	802	0.719	6′ 18″	6.67
	Min.	20	3.80	8.14	12.18	2.21	2.66	696	0.686	4′ 57″	6.55
	Ave.	32	4.26	8.48	12.74	2.40	2.89	744	0.698	5′ 42″	6.63
Reported analyses			4.25	9.68	13.93		3.65	793			
SEPT.	Max.	46	4.90	8.62	13.33	2.62	3.15	800	0.699	6′ 11″	6.69
	Min.	17	3.30	7.87	11.28	2.05	2.49	634	0.674	5′ 19″	6.64
	Ave.	32	4.19	8.25	12.44	2.32	2.79	728	0.687	5′ 36″	6.67
Reported analyses			4.11	9.44	13.55		3.69	777			
OCT.	Max.	47	4.95	8.18	12.60	2.40	2.89	776		5′ 36″	
	Min.	23	3.24	7.72	11.18	2.00	2.41	631		4′ 17″	
	Ave.	35	3.81	7.96	11.75	2.16	2.61	680		5′ 05″	
Reported analyses			3.81	9.03	12.84		3.29	725			

[1]Analyses made by N. P. Tarassuk and Miss M. A. Ashenfelder.
*Calculated on basis of 4,220 Calories per pound fat, and 1860 Calories per pound solids not fat (Ill. Agr. Exp. Sta. Bull. No. 308, 1928).
†Kahlenberg and Voris. Jour. Agr. Research 43: No. 8, p. 751, 1931, Table II.

mayonnaise jar, special jars 2 3/16 inches in diameter having flat bottom and straight sides were procured. Cut-off rain gauges were found very satisfactory. For the coagulant, rennet extract was found not only to yield results very similar in value to the pepsin-calcium chloride mixture described by Hill, but also gave less trouble in securing duplicate readings and less "piling" with certain milks. Fresh rennet was kindly furnished monthly by Chr. Hansen's Laboratory, Inc. When kept cold these samples were found to decrease only very slightly in strength during the month. One c.c. of rennet extract was quickly added and stirred into 100 c.c. of milk. Clotting in the case of unheated milk is almost instantaneous. Since 37.5° C. is not only closer to the optimum temperature for rennin coagulation, but also more nearly approximates body temperature than 35° C., it seemed desirable to employ the former temperature during the rennin action. This was followed during the month of April. However, because the curd test at the higher temperature is a few grams higher than at the lower, in order that these tests should be comparable with those already reported, it was decided to employ the lower temperature throughout the remainder of the study.

TABLE II

CURD TENSIONS OF VARIOUS FORMULAS

RAW LOW TENSION MILK OZ.	KARO TBSP.	WATER OZ.	CURD TENSION		
			RAW GRAMS	BOILED 3′ GRAMS	BOILED 10′ GRAMS
14	2	–	27	13	13
15	2	–	30	13	12
16	2	–	32	10	6
16	3	–	19	3	1
18	3	–	28	13	7
20	3	–	36	11	11
14	2	10	8	7	7
15	2	9	10	6	6
16	2½	8	8	9	10
18	3	6	14	7	7
20	3	5	17	11	9
RAW CERTIFIED MILK	KARO	WATER	RAW	BOILED 3′	BOILED 10′
14	2	–	38	5	3
15	2	–	40	9	7
16	2	–	58	9	9
16	3	–	46	7	4
18	3	–	35	11	10
20	3	–	45	10	10
14	2	10	16	7	6
15	2	9	17	6	9
16	2½	8	23	8	9
18	3	6	27	10	10
20	3	5	31	11	9
EVAPORATED MILK*	KARO	WATER	RAW	BOILED 3′	
Blank	–	–	4	4	
15	2	–	3	3	
15	2	9	3	3	
RAW MARKET MILK†	KARO	WATER	RAW	BOILED 3′	
Blank	–	–	87	14	
15	2	–	73	9	
15	2	9	28	7	

*Reconstituted 1:1. Final analysis: Fat 3.0%; S. N. F. 10:32%.
†Random sample: Fat 4.4%; S. N. F. 8.97%.

In making the tests reported in Table II, in which the effects of dilution, addition of syrup, and heating were studied, it was necessary to add calcium chloride to obtain rapid clotting especially in the heated samples. Hence, the unmodified Hill test, excepting the jars, was employed throughout that series of observations.

In making the readings the balance was mounted in a vertical position over a movable platform. The jar with its contents was placed on the platform, the balance was attached to the knife and the platform was slowly and carefully lowered until the knife was drawn through the curd.

That there were considerable fluctuations in the composition of the milk from time to time is indicated by the wide differences in maxima and minima (Table I). As stated before, precautions were taken to guard against this occurrence, especially in connection with the selection of animals, their care, feed, and the handling of the milk. Frequent tests of the milk from the individual cows, however, showed definite variations, making it necessary to replace certain animals with others, or in making up the supply of mixed milk to use only a minimum quantity of the milk of that animal yielding milk of highest curd tension. The maximum values, therefore, appeared as seldom as possible throughout the period, usually not over two or three times in any one month. Changes in climatic conditions unquestionably played an important rôle in inducing variation in the percentage composition of the milk.

While as yet no well-defined quantitative relationship can be established between the curd tension and the percentage composition of the milk, yet the fluctuation in the latter (Table I) is usually reflected in the fluctuation of curd tension. The term "soft curd" is as yet not uniformly defined, but it is felt that the milk used throughout this study with the exception of those few samples already referred to is representative of "soft curd" milk.

Little comment needs to be made in connection with the fat content of the milks, but inspection of Table I reveals that the average percentages of solids not fat are considerably below what are considered normal for the breed for the corresponding fat content. This is quite apparent when one compares the average values for each month with the analyses reported by Kahlenberg and Voris on the milk from 12 Holstein-Friesian cows over the entire lactation period. It may also be observed that the concentration of protein in this low-curd tension milk is low when compared with that of the mixed herd milk of similar fat content.

From the nutritional point of view it is to be expected that milk whose major constituents (or any of whose major constituents) are lower in concentration than in mixed herd milk would be lower in energy value. That this is true is apparent when one compares the calculated energy values of the monthly average with those of herd milk of similar fat content. It will be seen that the milk of low curd tension

on the average was from 5 to 6 per cent lower in energy value than the herd milk. This was significant in compounding formulas for infant feeding as will be seen later (Clinical Study).

While there was considerable variation in the percentage of ash in the milk, yet the average values approximate closely those accepted as normal for the breed. From the nutritional aspect, little or no significance would be attached to this variation since it is known that cow's milk is abundantly rich in mineral constituents, and that the elements, calcium and phosphorus, are almost universally present in a constant ratio. It is recognized, however, that the mineral constituents do play an important rôle in connection with the buffer capacity of milk, especially as regards acidification.[6] Electrometric titrations were made on representative samples of this low tension milk, and buffer curves were drawn. Buffer index values vary according to the P_H at which they are determined, but it was considered that the buffer capacity from the original P_H of the milk to a P_H nearing that of an infant's stomach at the height of digestion might be of some value clinically. Gonce and Templeton[7] have indicated that the latter value approximates P_H 3.75. Our buffer curves indicate that the buffer capacity of cow's milk is greatest between a P_H of 5.2 and 5.7 which is in agreement with that recently reported by Holm, Webb and Deysher.[8] For the sake of comparison with the results of the latter workers, the average buffer capacity from the original P_H of the milk to P_H 4.7 was calculated. The value of 0.0191 for the low tension milk, 0.0211 for the milk of two normal Holstein-Friesian cows, and 0.0196 for milk admittedly low in buffer capacity, the latter two values being reported by Holm, Webb and Deysher, indicate that this low tension milk is considerably below the normal milk of the breed in buffer capacity. A further comparison, shows that, whereas it required 52 c.c. of tenth-normal hydrochloric acid per liter to reduce the P_H of the normal Holstein milk from the original P_H to P_H 4.7, only 46 c.c. were required to effect a similar change in the low tension milk. Similar differences would be expected if the acidification were continued to P_H 3.75.

Table II illustrates what is to be expected when various feeding formulas, with and without heat treatment, are subjected to the curd test. The heating was done over a rapid electric heater, and excessive loss of moisture was prevented by the use of an air condenser. Karo itself appears to have little or no effect on the curd tension of raw milk, while dilution, as is to be expected, exerts a pronounced lowering, especially at the dilutions greater than 10 per cent. The effect of heat on the proteins of milk is reflected very distinctly in the marked lowering of the curd tension by the boiling for 3 minutes and 10 minutes, the longer period of heating having little or no advantage over the shorter. The effect of boiling is increased with increased concentrations

of Karo, due in all probability to the increased boiling point of the mixture. In the case of the reconstituted evaporated milk neither dilution nor heating exerts an appreciable effect on the curd tension.

CONCLUSIONS

1. Although different cows are known to secrete milk of varying curd tension, it has not been our experience that an individual cow invariably continues to secrete milk of a uniform curd tension throughout the major portion of her lactation period.

2. The prevailing opinion that normal milk of low curd tension is low in solids not fat, notably in proteins, has been confirmed.

3. Normal milk of low curd tension is low in energy value.

4. The buffer capacity of normal milk of low curd tension is less than that of milk of average composition.

5. Milk of low curd tension may be entirely normal with regard to physicochemical properties, such as rate of rennin coagulation, and P_H, as well as in bacterial flora.

6. The heat treatment accorded the various formulas in connection with infant feeding is effective in producing a mixture of very low curd tension, at least as far as average market milk is concerned. Prolonged boiling appears to have little or no advantage over the shorter period. The heating of mixtures in which evaporated milk replaces the raw milk is not effective in lowering the already very low curd tension of the mixture.

PART II. CLINICAL APPLICATION

The feeding of infants on the soft curd milk was carried out in the nursery for newly born at the University of California Hospital and at the Babies Aid Foundlings Home. Both institutions are located in San Francisco. While the period of observation in the nursery was relatively short, many of these babies are discharged as foundlings to the Babies Aid where they may remain for some time awaiting adoption. One of us (M.M.) being in charge of the latter institution, observations in both institutions could be made by the same physician over a group of infants for a period of six weeks to six months. Infants not born in the University Hospital but admitted to the Babies Aid were also given this special feeding. The age on admission of this latter group varied from six days to two months. These infants were under observation for two to eight weeks. Under the physician's guidance the same nurses aided in making certain observations as they weighed, fed, and cared for these babies. It was felt that this arrangement made for much more reliable and uniform conditions than would obtain in the average clinic or outpatient department. It was also obvious that in contrast with the group reported by Elias our age group was limited to that important period in infant feeding, under eight months. Included in the study were

babies whose initial feeding had not been under our direction, whose inheritance was not the best and whose environment had been poor. The variation in birth weight and lowered resistance to infection must be considered in reference to conclusions. Comparison, however, is made with much the same type of baby fed on evaporated and certified milk formulas.

We observed 60 babies on soft curd milk, but as brought out previously, the length of observation varied considerably. To make our results of any value we secured the help of a trained statistician. At her suggestion it was decided not to include the findings during the first week in the eleven cases which were put on soft curd at birth. The small number of calories consumed the first few days, and the initial loss of weight, were elements which would affect our conclusions. The

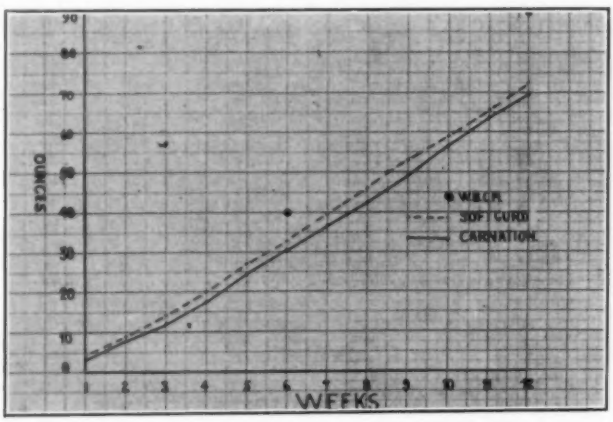

Fig. 1.

observations during the first week of life on babies started on soft curd milk before the eighth day have therefore been discarded in order that these cases might be included in this statistical study. For this same reason the cases followed longer than 56 days were also omitted as the number was so small that the statistical data would be rendered unreliable. These statistical studies have consequently been limited to a consideration of 44 cases observed over a seven-week period. In our histograms for comparison these regulations were also taken into consideration.

The average age of the start for infants fed on soft curd milk was 17.7 days with an average weight of 7 pounds, 6½ ounces. That of infants fed on evaporated milk was 19.9 days with an average weight of 7 pounds, 9 ounces. Therefore, on the whole, these children had recovered their birth weight. (Fig. 1.)

DISCUSSION

The graph in Fig. 1 shows a slightly greater constant gain, for infants fed on soft curd milk, than for those fed on evaporated milk. Although our data on undiluted boiled certified milk covers the period

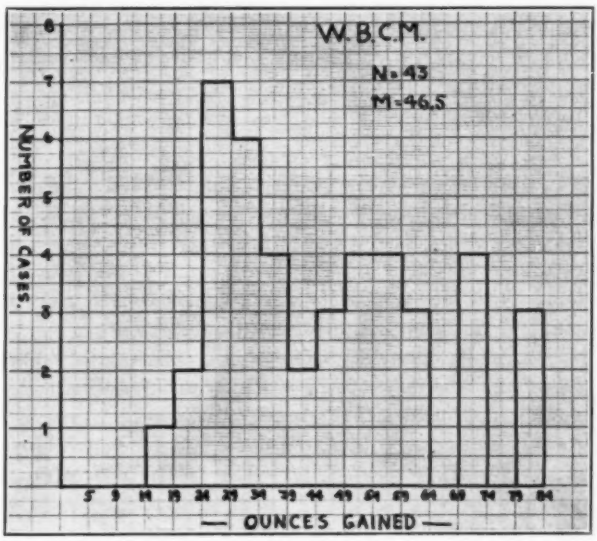

Fig. 2. Graph 1.

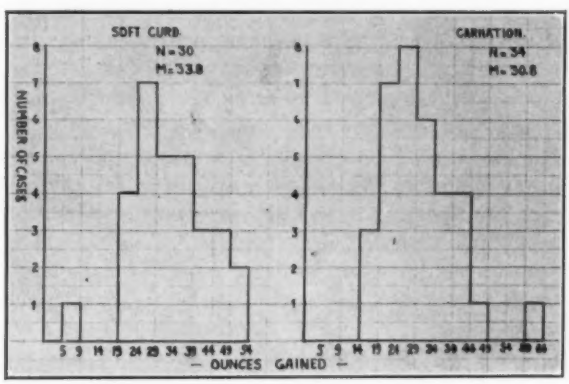

Fig. 2. Graph 2.

including initial weight loss, which is not included in either of the other groups and is hardly comparable, the gain in weight for the babies thus fed was much greater than for those fed on either soft curd or evaporated milk. The apparent difference in the gain of weight, of infants fed on soft curd milk over those fed on evaporated milk, has

been tested statistically by the standard deviation of the difference of means. It was found that this difference is insignificant, because the expected difference is greater than the observed difference.*

The histograms (Fig. 2) of the distribution of the total gain of weight on the different formulas are offered for comparison, although as was mentioned previously, our series on the undiluted boiled certified milk formula is not altogether comparable, as it includes the initial loss of weight after birth. (Fig. 2, Graph 1.)

From these histograms of weekly gain distribution the following are to be observed:

1. A very good distribution of weekly gain in weight by infants fed on both soft curd and evaporated milk.

2. A slightly greater constant gain for infants fed on soft curd than for those fed on evaporated milk.

3. The range of variation for evaporated milk babies is apparently less than it is for infants fed on soft curd milk.

4. With the exception of one case fed on soft curd milk there were no losses after the fourth week for either type of feeding.

5. An interesting observation is that eight cases or 18 per cent out of 44 infants fed on soft curd milk showed a loss of weight during some one of the six weeks, and that 14 babies or 33 per cent out of 42 evaporated milk fed infants showed a similar loss.

From a clinical point of view the infants on soft curd milk gained as well as a similar group on evaporated milk, but not as well as those on undiluted certified milk. The gain was usually gradual, and consistent. It was exceptional if a loss was incurred after the child was well started. However, from our clinical experience in infant feeding the group as a whole impressed us as being consistently hard to start artificially, when one took into consideration weight, comfort, and satisfaction. The babies were always hungry until they received from 42 to 95 calories per pound of weight or an average of 58 calories. It was the exception for a patient to be satisfied before receiving from 2 to 3 ounces of milk per pound of body weight. To make up the caloric intake necessitated adding from 8 to 11 per cent of carbohydrates. This increased requirement was also noted by Elias. It may also be explained by the lower energy value as reported in Part 1. An added reason for this higher feeding might also relate to the more frequent and copious stools. The average number of stools was from 4 to 6 a day, always soft and voluminous. They had the characteristics of a mother's milk stool, like scrambled eggs with soft fat curds. These, however, became smoother in consistency as the baby became accustomed

*The real difference is 33.8 minus 30.8 which equals 3, and the square root of the difference of these means is 5.54. Therefore, the difference in the variation around the mean as great as this could be expected within the realm of probability; i.e., in any series of cases under similar conditions one might expect to find as great a variation as was found in these cases.

to the formula. Contrary to the results of former observers the majority of our babies, or 79.1 per cent, passed large protein curds in the stool at various times, although their discomfort seemed in no way related to the passing of these curds. Regardless of the increased number of stools and the amount of carbohydrates in the formula, excoriation of the buttocks was not observed.

In the beginning we felt that these babies had more gas than the certified milk infants, this being the reason for their discomfort. As our experience increased and the infants were given more to eat, this discomfort diminished and gas became a negligible factor. It has been claimed that because the curd of low tension milk is soft and flocculent it is possible to give this milk undiluted and unboiled to the youngest baby, even to a weak premature baby. This may be a fact, but it is surprising how long the average baby took to accommodate himself to this milk, three weeks often passing before he was satisfied. We have fed about equal numbers on diluted and undiluted formulas, 22 of the former and 18 of the latter and find no appreciable difference. This is somewhat surprising if curd tension is so large a factor in the digestibility since dilution reduces still further the curd tension of milk (see Table II). Four of the babies who failed to gain and were unhappy on undiluted milk became comfortable and immediately gained when the same formula was diluted. Our intention was to use only unboiled milk, but on losing two babies after a 24-hour illness, sixteen cases were put on boiled diluted milk. The babies taking this formula were happy and satisfied and gained as well as the babies of the other two groups. It might be of importance to note that the stools in this group numbered only one to three a day and were much firmer and smoother.

The impression regarding tissue turgor was that babies who did well on soft curd milk invariably had hard and firm tissues. This might be due to the relative amount of lactalbumin which is theoretically of greater nutritional value. (See Table I.)

SUMMARY

A group of 60 infants ranging from birth to six months of age were fed on soft curd milk for a period of time ranging from 2 to 8 weeks. For statistical study the results of 44 infants thus fed and observed over a seven-week period were compared with results in similar groups fed undiluted boiled certified milk and diluted evaporated milk formulas. Histograms are presented for graphic comparison. When fed to the point of satisfaction, infants require more soft curd milk than ordinary cow's milk, due probably to the lower energy value of the former.

Clinical impressions suggest that while not superior to other accepted formulas, soft curd milk is difficult to start, but when well started is

very satisfactory and results in excellent tissue turgor. The stools of infants on soft curd milk are more frequent than those of boiled, diluted cow's milk and may often contain large casein curds.

CONCLUSIONS

Considering (1) the variability in the production of soft curd milk and the increased observation necessary in its production; (2) the lack of superior results when used in comparison with other accepted infant formulas, soft curd milk does not warrant special production and certification for use in infant feeding.

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POSTVACCINAL ENCEPHALITIS

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DANVILLE, VIRGINIA

HISTORICAL

IN 1905, Comby of Paris reported a case of encephalitis following vaccination. In 1912 another case was reported in the London Hospital. Mader reviewed a case observed in Germany in 1912. Luecksch of Prague in 1924 called attention to cases of supposed epidemic encephalitis following antismallpox vaccination. In 1924 Bastiaanse of Holland observed his first case. Five similar cases were observed elsewhere in Holland in the same month. In February, 1929, Wirsma of Denmark reported 11 cases of severe cerebral disturbances following vaccination. In the same month Levaditi of the Pasteur Institute, Paris, reviewed over one hundred cases occurring up to that time in Europe. The most severe outbreaks have arisen in Holland and England.

From the report of the Smallpox and Vaccination Commission of the International Office of Public Hygiene[1] the following more recent data concerning the distribution of postvaccinal encephalitis were obtained.

During 1923-1927, 139 cases of disease of the central nervous system following vaccination were described in Holland, of which 41 patients died. Many new cases have been reported since then. The ratio for the years 1923-1927 was one case to five thousand vaccinations, with a fatality of one in three. For the first six months, in 1928, the proportion was one case for each twenty-eight hundred vaccinations. For a period of five weeks, a vaccine from a country in which no case of postvaccinal encephalitis had been reported was used. A case occurred, however, with this lymph, in spite of the small number of vaccinations. The available data for England totaled about 130 cases. The ratio was one for forty-eight thousand vaccinations.

The report of a Commission in Germany covers a total of 102 cases. During the four-year period under consideration, for each million persons vaccinated the first time, there were nineteen disorders of the nervous system following the vaccinations, with seven deaths. For each million persons revaccinated, there was only one disorder of the nervous system with a fatal issue.

Sixty-five cases were reported in Austria. Twenty of these occurred in Vienna alone among 39,000 vaccinations. Twenty-nine cases occurred in Norway; 13 cases in Sweden; several cases in Czechoslovakia; a few cases in France and Switzerland; two cases in Soviet Russia; one case in Portugal, and one case in Jugoslavia. No cases occurred in Belgium, Spain, Greece, Italy, Poland, and Rumania. One

case has been reported from Canada, and one from South America since the report of the Smallpox and Vaccination Commission of the International Office of Public Hygiene.

The wave of this serious complication of vaccination began to recede gradually during the year 1929. References in the literature to new cases during the years 1930-1932 are scanty.

According to the delegate from the United States, as reported at Session of May, 1930, of the Permanent Committee of The International Office of Public Hygiene,[1] the total number of cases in the United States was about 20. Armstrong[2] states that 71 cases were recorded in the United States during the past ten years. Gordon and Rhea[3] recorded a case of postvaccinal encephalomyelitis in July, 1932. Roehm[4] reported a case in December, 1932, which he had observed in September, 1930. My own case, which occurred in February, 1930, is reported for the first time in this article. This would make a total number of 74 reported cases for the United States.

It is now thought that serious nervous complications of antismallpox vaccination have occurred in the past without having been recognized as such. In Germany an attempt has been made to reconstruct a great many such cases from the clinical and mortality records of vaccination cases. Some cases of postvaccinal encephalitis in the past are now believed to have been mistaken for tetanus.

ETIOLOGY

Since antismallpox vaccination constitutes the keystone in the arch of preventive medicine, one would expect a great deal of research and speculation on the cause of such a serious nervous complication as postvaccinal encephalitis and myelitis.

The early cases in Holland and in other continental countries occurred at a time when epidemic encephalitis was prevalent. It was thought that localization of the virus in the cerebral tissue inhibits the defensive power of the latter. This inhibition may unleash an encephalitis of the epidemic type in carriers or persons who already have a latent phase of the disease. It is a well-known fact that vaccine virus has a peculiar affinity for nerve tissue. Vaccine virus was demonstrated in the brain tissue in patients with encephalitis and also in patients who did not develop encephalitis.

Research by many investigators proved that the vaccine virus itself is not the cause of encephalitis. A neurovaccine, consisting of an emulsion of smallpox virus cultured in vivo in rabbits' brains, was used extensively on thousands of children in Spain without a single case of postvaccinal encephalitis. In Holland, one hundred and ten different kinds of lymphs were used and cases of encephalitis occurred after forty-one of these.

The Committee appointed by the Minister of Health and the Medical Research Council in England, under the chairmanship of Sir Hum-

phrey Rolleston, to report on the preparation and standardization of lymph, methods of diminishing or removing the risk of vaccination, and the best method of protection, does not incriminate any particular lymph. However, it is held that the vaccination virus, whatever its past history, and in whatever medium incorporated, initiates the nervous disturbance. A local individual predisposition to nervous disorders—in the widest sense of that term—is responsible for the unpleasant sequel to vaccination. This is as far as the British report goes.

An observation published later than the British report would seem to strengthen the theory that a local individual predisposition is responsible for postvaccinal encephalitis. Reisch[5] observed 2 fatal cases of postvaccinal encephalitis showing the characteristic histologic picture. During life, these patients had myoclonia affecting most of the voluntary muscles. A careful investigation of about 300 children in the same neighborhood revealed the presence of myoclonia in many, and in both the vaccinated and unvaccinated children to an equal extent.

Netter who has thoroughly studied this question discussed this subject before the Academy of Medicine in Paris.[6] He disregards the conception of some authors that a contaminated vaccine might be the cause of the encephalitis; and likewise, the views of others, who assume that a virus existed previously in the brain of the subjects and was enhanced in virulence by the vaccine. He contends that it is a question of an attack on the brain by the vaccinal virus, which can occur only in subjects with a nervous system that is particularly susceptible, and with a very active vaccine.

In 1927, when postvaccinal encephalitis occurred in alarming frequency in Holland, the law which decreed compulsory vaccination was temporarily revoked, and a committee was appointed to study the cause of this complication and the ways to combat it. The Committee published a report in 1932 which contains a thorough survey of encephalitis postvaccinalis.[7] Several hypotheses have been investigated, but no solution to the problem has been found. Encephalitis occurred with all kinds of lymph. Animal experiments to produce postvaccinal encephalitis failed.

In the discussion of the etiology two hypotheses are especially stressed. First, that the condition is due to the activation of a latent virus. Second, that the vaccine virus itself causes the disease. Neither can be regarded as proved. With this, it seems, our present knowledge concerning the causation of postvaccinal encephalitis rests.

Leiner of Vienna advanced the theory that encephalitis following vaccination was due to cerebral metastases. Weichsel[8] cites a case in a child, aged eighteen months, who developed a generalized vaccinia and encephalitis nineteen days following vaccination. This case is offered as a confirmation of Leiner's theory.

TABLE I

NO.	AGE	DAYS AFTER VACCINATION	FEVER	HEADACHE CONVULSIONS RIGIDITY OF NECK	LETHARGY UNCONSCIOUSNESS	REFLEXES	EYE SYMPTOMS	PARALYTIC SYMPTOMS	DURATION OF ILLNESS	RESULT
1	7½ yr.	7	Yes	Headache						Died
2		7			Lethargy			Immobility	19 days	Died
3	6 yr.	13		Headache Rigidity		Increased	Photophobia	Spasticity of extremities	17 days	Died
4	17 mo.	19	Yes	Convulsions				Left hemiplegia Spastic hemiplegia		
5	11 yr.	12	Yes	Headache Vomiting				Cranial nerve palsies	14 days	Died
6	18 mo.		Yes		Lethargy		Internal strabismus	Contracture of upper limbs		Recovered
7	13 mo.	6						General muscular rigidity Spastic paralysis		Mental deficiency
8	5 yr.	3	Yes	Headache Convulsions	Unconsciousness	Absent	Upward rotation and fixation	Weakness right arm and leg	4 days	Died
9	5 yr.	13	Yes	Headache Rigidity of neck	Lethargy		Ptosis right upper lid	Spasm of left side of body	15 days	Died
10	2 yr.	7	Yes		Unconsciousness		Both eyes turned to right	Weakness of left leg		
11	12 yr.	12			Lethargy	Anomalies			16 days	Recovered
12	21 mo.	10			Unconsciousness	Anomalies		Facial paralysis left side Spasm of extremities	28 days	Recovered
13	5 yr.	2	No	Headache Rigidity of neck	Lethargy		Internal strabismus; ptosis of upper right lid		26 days	Recovered

CLINICAL MANIFESTATIONS

According to Flexner,[9] the two immediately arresting features of postvaccinal encephalitis are its hyperacute course and its high fatality. Prodromes including headache, vomiting, and pyrexia, plus paralysis, are regarded by the English as the cardinal symptoms of postvaccinal encephalitis.

According to Armstrong[2] rigidity of the neck has been quite constant in American cases. The local vaccinal reaction has no peculiar character in the children who develop encephalitis.

Until recently, it was believed that the occurrence of encephalitis after vaccination which locally had no result; i.e., a vaccination without a successful local "take," could be excluded. However, the disease was described[10] in a child, aged thirteen years, which began five days after a revaccination and which was characterized by respiratory and nervous symptoms without any local reaction from the vaccination. After four days, the child died. Examination of the nervous system demonstrated lesions greatly resembling those found by others in cases of encephalitis postvaccinalis.

Recovery, when it takes place, tends to be complete. The outcome is independent of the stormy course and alarming character of the disease at the outset. Sequelae are very rare, and are in striking contrast with the end-results in cases of epidemic encephalitis of all grades of severity.

The clinical picture is not uniform. It may be that of tetanus, tuberculous meningitis, poliencephalitis or an obscure form of general intoxication, not typical enough even to suggest encephalitis.

The recorded observations on 13 cases of postvaccinal encephalitis are presented in tabular form.

PATHOLOGY

The pathologic findings in the brain and cord establish postvaccinal encephalitis as a clinical entity. According to Flexner[9] even the gross appearance of the brain and cord in postvaccinal encephalitis differs from epidemic encephalitis. The lesions as disclosed by the microscope are more impressively distinct. The characteristic type of lesions in epidemic encephalitis is proliferative and infiltrative.

The findings in postvaccinal encephalitis consist of adventitial and periadventitial round-celled infiltrations distributed throughout the brain and cord. With appropriate staining methods, areas of myelin degeneration may be seen centered about the smaller vessels, which gradually fade into normal myelin structure. The characteristic softening or microglia proliferation about the blood vessels of the white substance of the central nervous system resembles the action of a toxic substance.

As compared with epidemic encephalitis, in which the lesions are nearly always confined to the brain, and chiefly to the basal gray matter, with much rarer involvement of the cortex and white matter, postvaccinal encephalomyelitis is a disease in which both brain and spinal cord and both the gray and white matter of each, are implicated; and in which the white matter is attacked by preference. The brain and cord are diffusely affected, often without any particular choice of locality, though not everywhere with the same intensity. The lesions in the spinal cord are as important as those in the brain, if not more so.

It is a remarkable phenomenon that with lesions so widespread and severe in fatal cases, complete functional restoration takes place, as a general rule, in those that recover.

There are no characteristic blood and spinal fluid findings in this disease. German observers[11] found smallpox virus in the blood of 8 children between the third and tenth days after vaccination with reaction, and absent from the blood of 9 others. None of the spinal fluids obtained from the children contained virus, even when it could be demonstrated in the blood. The spinal fluid of one of the three infants with symptoms of postvaccinal encephalitis produced by the same vaccine, contained virus on the twelfth day after vaccination. The reports of other observers on the spinal fluid show essentially negative findings. The fluid is sterile, and at times, increased in pressure. There may, or may not, be a slight increase in the cell count. One case showed one hundred and seventy-nine cells per cubic millimeter. Tests for globulin were normal in some spinal fluids, while negative in others. Qualitative tests for sugar were positive in all the spinal fluids tested.

According to a Dutch authority,[12] the following points characterize postvaccinal encephalitis and differentiate it from epidemic encephalitis.

EPIDEMIC ENCEPHALITIS	POSTVACCINAL ENCEPHALITIS
1. Thick layers of lymphocytes and a certain kind of plasma cells in the perivascular lymph spaces.	1. Accumulations of microglial granulated cells outside the perivascular lymph space in the nervous tissue itself.
2. Neuronophagia by glia cells, of which only a few were changed into granulated cells.	2. No neuronophagia.
3. Preference for the gray substance.	3. Strong preference for the white substance.
4. Diffuse spreading.	4. Spreading in concentrated heaps.
5. Preference for the brain trunk.	5. Preference for the hemispheres.

PREVENTION

Considering the number of antismallpox vaccinations performed yearly, the chances for serious nervous system complications are infinitesimally small. However the total number of such complications

is rather impressive, and may serve as a tool in the hands of various antivaccinationist elements. It may justifiably cause some concern to the regular medical practitioner.

While the problem of etiology is still unsolved, yet sufficient facts of epidemiologic nature have been accumulated to constitute a rational basis of prevention.

The important fact has been noticed that in countries where vaccination is practiced in infancy none, or very few cases of encephalitis, have developed. Also, the number of cases of encephalitis following revaccinations is smaller than that following primary vaccinations. On the basis of these facts, the English Committee recommends that primary vaccination shall be performed in infancy between the ages of two and six months, and revaccination at the time the child enters school, five to seven years, and again on leaving, fourteen to sixteen years. In place of the officially advocated four insertions, trial shall be made of vaccination and revaccination in one insertion. Multiple scarification and cross-hatching are depreciated. The Minister of Health is of the opinion that it is not generally expedient to press for the vaccination of persons of school and adolescent age who have not previously been vaccinated, unless they have been directly exposed to infection.

Sixty-six per cent of all cases of postvaccinal encephalitis in England occurred between the ages of five and fourteen. Seventy-nine per cent occurred in persons between the third, fourth, and fifth year of life. Infants under one year of age are relatively nonsusceptible to postvaccinal encephalitis.

In Holland, during the period covered by the report, among 14,038 vaccinations from birth to one year, 1 case occurred. Among 32,865 vaccinations between the ages of one and two years, 1 case occurred. In 1,879 vaccinations, between the ages of one and eleven years, 1 case occurred. This confirms the relative nonsusceptibility of young children.

In the countries where postvaccinal encephalitis occurred, it affected children mostly of school age; only rarely has a case occurred in infants under two years.

Knoepfelmacher states that not a single case of postvaccinal encephalitis has occurred among persons vaccinated by the intradermal method of Leiner. However, it was impossible to ascertain the number of persons who were vaccinated by the intradermal method of Leiner, on the basis of which the conclusion of Knoepfelmacher was made.

In connection with prevention of postvaccinal encephalitis, the work and views of Armstrong[2] merit the widest circulation and extensive clinical application. What follows is a condensation of the views of Armstrong.

Judicious exercise is essential for the fundamental well-being of familiar tissues, even to the bones and teeth. It may be assumed that the same is true of those tissues which constitute the defense mechanism, whatever and wherever they may be. Armstrong decided to determine whether preliminary immunization by the injection of nonspecific antigens might increase temporarily an animal's efficiency in its reactions against a subsequent inoculation with vaccinia. This conception squares fully, or is identical with, the principle of nonspecific protein theory. The parenteral administration of a nonspecific antigen influences a subsequent infection. Similarly, an acute infection may favorably modify the course of a chronic infection. The "nonspecific" stimulation of the defense mechanism constitutes the exercise for the defense mechanism which may be utilized therapeutically and prophylactically.

Armstrong attempted to verify experimentally the hypothesis that previous nonspecific inoculations would render an animal's response to vaccinia more efficient. He made use of a strain of vaccine virus developed at the National Institute of Health, which was capable of producing a fatal meningo-encephalitis when introduced into the brains of white mice. A dose of virus was selected through preliminary titration which was slightly less than sufficient to kill all of a group of normal mice. Preliminary to the intracranial inoculations with the most fatal vaccine virus, the mice were immunized against various antigens; diphtheria toxoid having been mainly used as the antigen. He then compared the number of deaths among previously immunized and nonimmunized groups following intracranial inoculation with vaccine virus. In each experiment, mice for the test and control groups were from the same shipment, and were placed under identical conditions.

The investigation showed that there were more survivals in the toxoid-immunized groups than in the other groups; and that the toxoid-treated mice tended to die later than the controls. The results indicated that the protection afforded by a previous nonspecific stimulation is only relative, and not absolute. However, the test was a very severe one since the vaccine virus was injected into the brain tissue itself, thus shunting out whatever mechanism there exists for protecting the central nervous system against vaccine introduced by other routes than into the central nervous system itself.

While the protection of a few mice from a cerebral virus infection by means of a previous nonspecific stimulation of the defense mechanism does not necessarily lead to the conclusion that children could similarly be protected from postvaccinal encephalitis, yet the conception on which the work of Armstrong is based, and the limited amount of experimental laboratory evidence to support it, is sufficiently sound to accept its implications in practice.

Armstrong recommends that primary vaccinations, especially after the first year of life, be deferred until contemplated immunization against diphtheria or other diseases has been accomplished. The recent preliminary exercise of the immunity or defense forces may lead to a more efficient antivirus response, with the result that the ensuing reaction may tend to simulate primary infant, or secondary, vaccinations in their comparative mildness and freedom from post-vaccination reactions.

Since immunization against diphtheria is now almost universally practiced in this country, it would be of value to put Armstrong's ideas and work to the widest clinical trial.

TREATMENT

In the absence of a definitely established cause of postvaccinal encephalitis, treatment must necessarily be empiric. Epidemiologic observations, however, furnish us with some facts on the basis of which certain broad prophylactic measures may be formulated. From the reports of the various commissions on this subject the following is adduced with regard to prophylaxis.

1. Postvaccinal encephalitis is much less frequent in young children than in older children.

2. No person should be vaccinated unless he is in perfect health.

3. Primary vaccination should be performed during the first year of life.

4. Secondary vaccination should be performed after ten years of age.

5. Attenuated vaccines should be used.

6. Only a single superficial skin insertion or puncture should be done, with a minimum of trauma.

7. When a postvaccinal central nervous system complication follows, it is infinitely less grave when it follows a vaccination made during the first months of life.

Therapeutically favorable results were reported from the use of blood serum from recently vaccinated persons. However, the good results were not always uniform. Hekman[13] had the opportunity to observe the therapeutic results of blood serum treatment simultaneously in two children aged two and four, respectively. When the child aged two was admitted to the hospital, seven days after being vaccinated with cowpox, it had spasms over the whole left side of the body. Both eyes were turned constantly to the right; also the head. During the attacks, the face was pale and cyanotic. The child was unconscious, and the pulse was rapid—about 140. On the left upper arm were three distinct pox pustules with considerable reaction in the vicinity. The evening of the day of admission, the patient received

an intravenous injection of 10 c.c. of blood serum from the mother, who had been vaccinated at the same time as the child. The following day, the injection was repeated. The morning of that day the patient had still a few attacks, but toward noon they ceased. The child was, however, still unconscious, but the temperature began to fall, and in two days it had become normal. Twelve days later, the patient was dismissed as cured. The other child, aged four, received similar treatment but died, in spite of repeated injections of serum.

The British Report contains numerous observations on the efficacy of serum treatment. While serum treatment should be undertaken in every case, the exceptions are too numerous to regard it as a specific measure.

CASE REPORT

J. L., five years of age, third child. Full term, normal delivery. Birth weight, eight and one-half pounds. Breast fed. History of whooping cough, measles, chickenpox, and occasional attacks of tonsillitis.

The child was vaccinated for smallpox on January 24, 1930. One or two days after vaccination, he began to complain of pain in his stomach and head, but he had no fever. Three days after vaccination, he began to vomit. There were no diarrhea, fever, chills, or cough. He lost weight rapidly, and gradually began to appear indifferent and drowsy. He complained of pain in the back only when moved.

The child was first seen Feb. 7, 1930, two weeks after vaccination. He was a well-nourished boy, but somnolent, and answered questions slowly and with difficulty. Examination revealed a scaphoid abdomen; slightly positive bilateral Kernig signs; neck very rigid and painful on moving; generalized hyperesthesia of skin; internal strabismus and ptosis of right upper lid; pulse rate about seventy-five. Urinary findings were negative.

Lumbar Puncture. Eighteen cubic centimeters of clear fluid were withdrawn under considerable pressure. Cell count, one and one-half hours after withdrawal, was 15 to 20 per cm., consisting entirely of lymphocytes. Tests for globulin were positive. Qualitative test for sugar was positive. Ophthalmoscopic examination revealed normal eyegrounds.

Child gradually improved. Twenty-six days after the onset of symptoms, the child was well, with the exception of slight ptosis of the upper right lid, which disappeared a few months later.

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PHRENIC NERVE PARALYSIS IN THE NEWBORN, ASSOCIATED WITH DUCHENNE-ERB'S PARALYSIS

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UNILATERAL paralysis of the diaphragm in the newborn has been but rarely reported, only nine such cases being found in the literature. Of these, seven alone were associated with simultaneous paralysis of the brachial plexus.

Weigert[1] in 1920 collected thirty cases of unilateral phrenic nerve paralysis from the literature, with one of his own, but only two of these were in newborn infants, and in no case was there verification by fluoroscopy.

It is not my purpose to discuss paralysis of the diaphragm in older children—due to tuberculosis, trauma, pressure on the phrenic nerve from various causes, diphtheria, or poliomyelitis—but to confine this study to the type of paralysis affecting the newborn. Accordingly I have brought together all reported cases, tabulating and summarizing them for ready reference. To the cases reported two are added that have come under my personal observation.

The phrenic nerve, which is principally motor, has its origin mainly in the fourth cervical nerve, but receives additional fibers from the third and fifth cervical nerves, this last-named association bringing it into the domain of the brachial plexus, among the supraclavicular branches of which is one which communicates with the phrenic nerve. The nerve runs down the neck on the scalenus anterior muscle, crossing this from without inward, and at the base of the neck accompanies it between the subclavian artery and vein. Entering the thorax it passes over the root of the internal mammary artery, from within outward, then follows an almost vertical course downward over the apex of the pleura and through the superior and middle mediastina to the upper surface of the diaphragm, which it supplies with muscular branches. The right phrenic nerve is shorter than the left because of its more direct downward course and the greater elevation of the diaphragm on that side. Both nerves break up into terminal branches before reaching the thoracic surface of the diaphragm; some of the branches of the right nerve, the phrenicoabdominal, traverse the diaphragm and pass to the muscle from the under surface.

From our knowledge of its anatomy, it is easy to understand how in a typical case of Duchenne-Erb's paralysis the phrenic nerve may

From the Pediatric Department of the Brooklyn Jewish Hospital.

readily be damaged at the same time that the plexus has been injured at birth, whether the lesion be due to difficult or forceps delivery or to breech delivery.

REPORT OF TWO CASES

CASE 1.—Baby K., a boy, weighing 9 pounds 8 ounces at birth, which was by breech delivery, was seen at the office two weeks after delivery, June 21, 1928, suf-

Fig. 1. Case 1.

fering with a cough and dyspnea. Physical examination revealed a large, well-nourished infant, with a Duchenne-Erb's paralysis on the right side, together with a hematoma of the sternocleidomastoid muscle. No cyanosis was present. The respiration was rapid, and there was slight dullness at the base of the right lung, with diminished breathing. No râles were heard.

On fluoroscopic examination the heart was seen to be pushed somewhat over to the left side. The diaphragm on the right side appeared high and exhibited the characteristic "paradoxical movement" first observed and named by Kienbock in 1898 in a case of pyopneumothorax: The right half of the diaphragm moved

up with inspiration, contrary to what occurs in normal respiration, while the left half moved down in the usual way, thus showing a typical see-saw action, since known as *Kienbock's phenomenon*. Roentgenograms of the chest at this time revealed that the right diaphragm was markedly raised, being at least two intercostal spaces higher than the left, and that the abdominal viscera were raised proportionately with it, while the heart was slightly displaced to the left. There was no evidence of diaphragmatic hernia. Repeated fluoroscopic examinations showed that within one month the diaphragm had receded to its proper place. One year later roentgen examination revealed a completely normal relationship between the right and left sides of the diaphragm. The child has subsequently developed normally in every way, and the Erb's palsy has entirely cleared up.

CASE 2.—Baby L. M., a case of high forceps delivery, with weight 7 pounds 2 ounces at birth, was brought to the office two weeks later with a history of cyanosis. The essential physical findings were as follows: Right-sided Duchenne-Erb's paralysis; slight cyanosis, rapid respiration, dullness and diminished respiration at the right base; no râles. Fluoroscopic examination revealed that the diaphragm on the right side was at least two intercostal spaces higher than on the left, with the characteristic see-saw action of the diaphragm. Roentgenograms confirmed these findings. One month later under fluoroscopy the diaphragm was seen in its normal position. Repeated examinations at subsequent dates showed a complete recovery from the right-sided Erb's palsy and the right phrenic nerve paralysis.

REVIEW OF THE LITERATURE

For convenience in summarizing the cases found in the literature, I have taken as a basis the tabulation drawn up by de Bruin,[2] making the necessary additions to include four more recent cases, and omitting the cases of Weigert[1] (1920) and Dyson[3] (1927), which do not properly belong here, since in neither of these was there an associated paralysis of the plexus. Incidentally, however, these two cases refute Epstein's[4] assertion that injury to the phrenic nerve without concurrent involvement of the brachial plexus has never been cited in the literature, and that one cannot conceive of such a phenomenon. Dyson's[3] case was accounted for by the fact that in cutting through the umbilical cord, which was wound several times around the neck, the latter was accidentally incised with direct injury to the phrenic nerve, resulting in paralysis of the diaphragm without an associated Erb's paralysis. Why in Weigert's[1] case the nerve alone should have suffered without the plexus sharing in the paralysis has not been explained.

A glance at our table shows at once that in every case the twofold paralysis followed a difficult labor or one with some abnormal feature. Thus in four cases there was forceps delivery, and in five cases breech delivery, suggesting beyond a doubt that the condition was the result of a trauma inflicted at the time of birth. It is worthy of note that the injury was located on the right side in seven of the nine cases—an observation which is of importance for differentiation from *relaxatio diaphragmatica*, which may also exist in the newborn. In all nine cases the diagnosis was confirmed by the roentgen rays.

It was Kofferath,[5] in 1921, who first reported a case of phrenic nerve paralysis in the newborn, associated with Duchenne-Erb's paralysis of the brachial plexus.

TABLE I

	R. OR L.	BIRTH	CLINICAL SYMPTOMS	ROENTGEN FINDINGS	RESULT	PLEXUS PARALYSIS
Kofferath (1921)	R.	37-yr. primipara. Low forceps. Episiotomy.	Dyspnea immediately following birth. Dilated alae nasi; thoracic type of breathing.	High position of diaphragm on right side; paradoxical movements. Heart pushed to left and downward upon inspiration.	Cured after 4 months. Cessation of paradoxical movements. Diaphragm still a little too high on right side.	+
Landsberger (1926)	R.	Breech presentation. *Veit-Smellie.*	Asphyxia, cyanosis; peculiar short respiration. Diagnosis: pneumonia. Symptoms appearing soon after birth.	High position of diaphragm on right side. Right half of diaphragm moderately movable.	Death from pneumonia 2 months after birth.*	+
Friedmann and Chamberlain (1927)	R.	Low forceps.	Attacks of cyanosis. Râles. Diagnosis: pneumonia. First symptoms appeared after 14 days.	Paradoxical movements. Diaphragm high on right side.	Plexus paralysis, cured in 14 days. Paralysis of diaphragm. Cured after 8 months; confirmed by roentgenogram.	+
Epstein (1927)	R.	Breech presentation. Difficult labor.	Rapid, irregular respiration immediately after birth. Right half of chest moved less than left half. Dullness and weak respiration. No râles.	Right half of diaphragm higher by 4 ribs than left. Paradoxical movements. Entire right lung in shadow.	Under observation until third year; 3 attacks of bronchopneumonia. Roentgenologic changes persisted.	+ (Soon cured)

*Autopsy: Diaphragm atrophic on right side. Fewer muscle fibers. Neither gross nor microscopic changes in phrenic nerve, brachial plexus or spinal cord. Atelectases and desquamative catarrah of right lung.

TABLE I—CONT'D

	R. OR L.	BIRTH	CLINICAL SYMPTOMS	ROENTGEN FINDINGS	RESULT	PLEXUS PARALYSIS
Mulzer (1928)	L.	Forceps. Long, tedious birth.	In this mild case no clinical symptoms.	Movements normal on right side; less movement on left. High position of diaphragm on left.	Rapid cure of N. phrenicus and plexus.	+
Remé (1930)	L.	Primipara. Breech delivery; difficult labor.	Rapid breathing, cyanosis immediately after birth. Abdomen contracted on inspiration. Became cyanotic upon crying.	High position of diaphragm on left side. Paradoxical movements.	Regression of plexus paralysis; persistence of phrenic nerve paralysis at age of 1 year.	+
de Bruin (1931)	R.	Second of a pair of twins. Breech presentation.	Pneumonia and pleurisy. Râles. Dyspnea.	High position of diaphragm on right side. Heart displaced toward left and downward.	Little change during 6 weeks of observation. Sudden death at age of 4 months. Cause unknown.	+
Stein (1933)	R.	Breech delivery.	Rapid respiration. Dullness at base. Hematoma of sternocleidomastoid muscle.	High position of diaphragm on right side. Paradoxical movements.	Diaphragm had resumed proper place in 1 month.	+
Stein (1933)	R.	High forceps delivery.	Cyanosis, rapid respiration, dullness and diminished breathing at right base.	High position of diaphragm on right. Paradoxical movements.	Diaphragm in normal position after 1 month.	+

This author sought vainly in the literature for another case of the same kind. He had noted soon after the birth of the child that respiration was unaccountably labored, and this observation, combined with evidence of injury from forceps at Erb's point, suggested to him that the infant was suffering with traumatic paralysis of the phrenic nerve. It was not until twenty-four hours later that the paralysis of the plexus also became evident, through a palsy of the right arm. The fluoroscope confirmed the injury to the phrenic nerve by revealing the classic paradoxical movement of the diaphragm. By the fourth day the paralysis of the nerve had passed, and respiration was normal. The plexus paralysis, however, slower to yield, did not disappear until the end of four months.

Two of the nine cases listed in the table terminated fatally. In that of Landsberger[6] in which the infant was delivered in breech presentation, pneumonia symptoms supervened soon after birth, to which the infant succumbed at the age of two months. At postmortem the diaphragm was found to be atrophic on the right side, and on microscopic examination it was seen to contain fewer muscle fibers than on the left side. This last finding furnishes definite proof that the case was not one of *relaxatio diaphragmatica*, which may equally be congenital and may present the same high diaphragm on the fallen side. A study of the phrenic nerve, brachial plexus and spinal cord revealed no changes either gross or microscopic in any of these structures.

In de Bruin's[2] case the infant, who was the second of twins, born in breech delivery, was brought to the clinic at the age of four weeks, with a history of coughing and persistent refusal to take nourishment. A swelling of the sternocleidomastoid and the presence of a Duchenne-Erb's paralysis, both on the right side, together with the fact of a good general condition in other respects, suggested a congenital malformation, until the fluoroscope demonstrated a wide difference in the position of the diaphragm on the two sides with a definite *Kienbock's phenomenon* and a pushing of the heart toward the left side and downward. The case was under observation for six weeks, and gradual improvement noted, when at the age of four months death suddenly occurred, the cause of which remains unknown since it was impossible to obtain an autopsy.

The predominant clinical symptoms of paralysis of the phrenic nerve are cyanosis, dyspnea and other respiratory disturbances, together with disorders of nutrition in less degree. Thus in all cases but one (Mulzer's[7]) the presence of pulmonary symptoms of one or another nature was recorded. In Epstein's[4] case the child, under observation until the third year, suffered three attacks of bronchopneumonia and the roentgenograms showed the lesions still persisting. The low forceps case of Friedmann and Chamberlain[8] likewise exhibited symptoms of pneumonia; but these did not appear until the plexus paralysis had been practically overcome, at the end of two weeks. Here the paralysis of the phrenic nerve persisted up to the eighth month, as was confirmed by roentgenogram.

Mulzer's[7] case, one of the two left-sided ones, was rather exceptional in that the phrenic lesion was entirely symptomless and might have gone undiscovered in the presence of an Erb's paralysis had not roentgenologic examination brought to light the high position of the diaphragm on the left side.

The case of Remé,[9] one of breech delivery, exhibited rapid breathing, cyanosis on crying and nutritional disturbances, which, according to that author, are of more importance when the lesion is on the left side. The fact of an Erb's paralysis of the left arm led to roentgen examination, which revealed the presence of a high diaphragm on the left side and the characteristic *Kienbock phenomenon*. In this child, at the age of three months, the chest was asymmetrical, with the left side more strongly arched than the right. The intercostal spaces were wider, and the ribs

took a more horizontal direction than those on the right side. When reexamined at the age of nine months, the paradoxical movement of the diaphragm and its high position on the left side were still persisting.

COMMENT

The clinical picture has been well described by Hitzenberger[10] in his special studies on the diaphragm. The great danger to which the patient is exposed, if the paralyzed nerve does not quickly recover, is that of pneumonia. The appearance of cyanosis and dyspnea shortly after an instrumental or difficult birth should lead the physician to suspect injury of the phrenic nerve. If such is the case, physical examination will as a rule reveal soon after birth extensive changes similar to those observed in massive pneumonia or pleurisy, but with normal temperature and a good general condition. Fluoroscopy will then disclose a high position of the diaphragm on the affected side and a typical paradoxical movement of the diaphragm (Kienbock phenomenon) in breathing, the affected side ascending during inspiration while the normal side descends, and the reverse of this, in expiration, like the see-saw appearance of a pair of scales in perfect synchronism. The respiration is irregular and rapid, and often there may be severe crises of air hunger. The type of breathing, unlike that of normal newborn infants, is thoracic. In Epstein's[4] case, the affected half of the chest made wider excursions in breathing than the healthy side. The heart is pushed out of place, toward the affected side and downward.

SUMMARY

1. The rarity of the cases reported arouses the question whether paralysis of the phrenic nerve is not more common in cases of Erb's palsy than has been supposed. The complete absence of symptoms in one of the cases reported confirms such a suspicion. Attempts to check up this phase of the subject have been unsuccessful, a number of newborn infants having been studied fluoroscopically for possible phrenic nerve injury, but no cases being observed.

2. A study of nine cases of phrenic nerve paralysis associated with Erb's paralysis discloses that the great majority of cases are on the right side.

3. The prognosis is favorable as regards restoration of function in the very early days of life, but appears to be less so if treatment is delayed two to three months. Even then the prognosis as to life is not unfavorable, as shown by the cases of Remé and Epstein.

4. Paralysis of the phrenic nerve should be looked for in all cases of Erb's paralysis.

5. The suggestion is made that, in view of Kofferath having been the first to describe the syndrome of Erb's paralysis with phrenic nerve paralysis, the name "Kofferath syndrome" be given to the condition.

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MYELOSARCOMATOSIS

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THE diversity of opinions as to the etiology and character of leucemia is fully recognized. Briefly, there are two schools of thought, those who believe in the infectious origin of leucemia and those who consider the disease a true blastomatous process. In favor of the former are the acute leucemias with abrupt onset, septic course, and short duration. In favor of the latter are the chronic leucemias with insidious onset, progressively downward clinical course and cellular infiltrations in the internal organs (Schultz[1]). To strengthen the view as to the neoplastic character of certain cases of leucemia are those rare instances of "complicated leucemia" such as chloroma and leucosarcomatosis in which the accumulation of leucocytes assumes the form and character of tumor. Recently I have observed clinically and at autopsy an obscure form of disease and have attempted to classify it. I believe this case falls into the group of "complicated leucemia" and appears to substantiate the blastomatous nature of certain forms of leucemia.

CASE REPORT

History.—M. S., a white boy, aged six and a half years, was admitted to Sarah Morris Hospital on March 27, 1931, with the complaints of swollen eyelids and sinus trouble of one week's duration and pain in the stomach of two weeks' duration. He was apparently well until December, 1930 when he developed a cold and sore throat. One week later he complained of drawing pains in the wrists, elbows, and anterior surface of the legs. The following day he experienced pain in the pit of the stomach, worse during the night and unaccompanied by nausea or vomiting. This pain disappeared spontaneously in twenty-four hours. Three weeks before admission to the hospital he contracted chickenpox during which time the bone pains disappeared. During convalescence from the chickenpox the bone pains and epigastric distress returned and persisted off and on up to the time of hospitalization. One week before admission his mother noticed swelling of his right upper eyelid. The following day the left side of his face was immobile and the left upper lid swollen.

The child's past history included measles at two years and frequent sore throats for which his tonsils and adenoids had been removed at the age of four years.

His grandmother (paternal) died of carcinoma.

Examination.—Examination revealed a well-developed but poorly nourished, extremely pale and emaciated child. His temperature was 100.4° R. Blood pressure was 108/70, pulse 130, and respirations 36. Scattered throughout his scalp were many round, pea- to marble-sized reddish purple nodules, firm in consistency and

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apparently attached to the underlying skull. They were most numerous over the parietal and frontal regions. He exhibited a left-sided peripheral facial paresis. At the middle of the lower margin of the right mandible a small rough bony elevation was felt. The eyes were prominent but did not protrude. Both upper lids were brownish pink, swollen and indurated but nonfluctuant. His lips were dry and his tongue was coated. The tonsillar fossae and pharynx were slightly injected. The anterior and posterior cervical lymph nodes were slightly enlarged, more on the left, and were discrete and firm. The heart and lungs were normal. The abdomen was scaphoid and the spleen was palpated just below the left costal margin. No other organs or masses were palpated. The genitalia were normal. Except for marked emaciation the extremities exhibited no abnormal findings. The axillary, epitrochlear, and inguinal lymph nodes were not palpated. There were no pathologic reflexes.

Laboratory Data.—

TABLE I

BLOOD FINDINGS

DATE	R.B.C.	HB	W.B.C.	POLY-MORPH.	LYMPHO-CYTES*	MONO-CYTES	EOSIN-OPHILES	BASO-PHILES	IM-MATURE R.B.C.
3/28	3.0	55	6200	44	48	6	2	0	0
4/8	2.78	55	8000	45	48	6	2	2	3
4/13	–	–	5000	23	68	3	1	2	1
4/18	2.86	55	12,200	45	49	0	2	1	0
4/22	–	–	10,000	48	46	6	0	0	2
5/8	2.67	50	12,500	80	11	8	1	0	8

*Many of the cells classified as lymphocytes were large. The nuclei were purplish in color, the chromatin rather dense, but not clumped as in the mature lymphocyte. Nucleoli were present and the nucleolar membrane was distinct. The cells contained abundant nongranular, sky-blue cytoplasm in which azurphilic granules were common (Wright and Giemsa stains). These cells might possibly be classified as "lymphoidocytes" (Pappenheim).

Chemical examination of the blood revealed normal nonprotein nitrogen, sugar, and cholesterol contents. Blood cultures on two occasions showed no growth. The blood Wassermann, Kahn, and the tuberculin tests were negative. Except for occasional granular casts the urine examination was repeatedly negative. Tests for Bence-Jones protein were negative.

Biopsy of Tumor Nodule of the Skull, April 7.—Microscopic examination revealed a new formation of cells extensively invading the bone and surrounding structures. The cells were small and round consisting of scanty acidophilic cytoplasm and round nuclei. The nuclei showed variation in chromatin content. Many mitotic figures were present. Marked vascularization of the tumor growth was present and many of the blood spaces were lined by tumor cells. Necrosis of the adjacent tissue was marked. The impression was that of a malignant tumor; lymphosarcoma, round-celled sarcoma, or leucosarcoma.

Course.—On March 31 x-ray examination revealed a peculiar mottling of the skull, particularly in the parietal bones, giving the appearance of having been "drilled by fine shot" (Fig. 1). The lower third of both femurs appeared moth-eaten (Fig. 2). There was also a similar rarefaction of the shaft of the fibula just below the head. Films of the entire pelvis and lower spine exhibited the same moth-eaten appearance. Films of the right arm disclosed erosion of the shaft of the humerus at the upper part of the lower third, and of the radius below the head (Fig. 3). On April 7 two nodules were removed from the skull for microscopic examination (see biopsy report). The nodules from the skull were reddish purple

in appearance, pea- to marble-sized, firm in consistency and involved the skin and underlying tissue. Secondarily, many of the nodules had undergone abscess formation. Two such abscesses, one from each eyelid, were incised. Gram-positive cocci were found on stained smear. From April 17 to April 20 many more nodules appeared on the scalp and over the back. At this time small, shotlike axillary and

Fig. 1.—Roentgenogram of the skull showing the moth-eaten appearance; the thinning and erosion of the cortex.

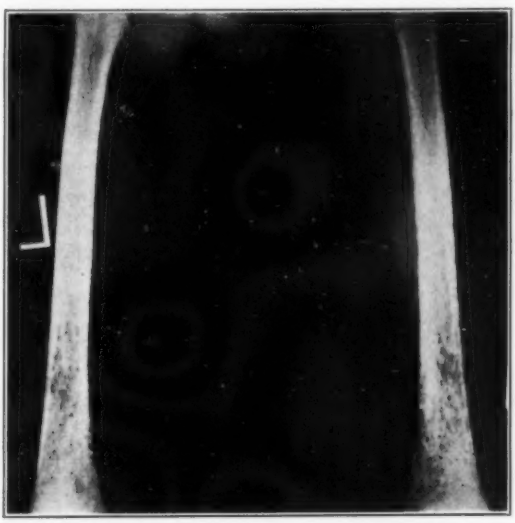

Fig. 2.—Roentgenogram of the femurs showing moth-eaten rarefaction in the distal portions.

inguinal glands were palpated. An x-ray of the chest on April 20 revealed no pulmonary neoplasm. The ribs, scapulae, and clavicles showed areas of rarefaction (Fig. 4). On April 27 left proptosis was present and the patient complained of pain in the left parietal region. On April 27 the patient received the first of several deep x-ray treatments to the skull and the long bones showing rarefaction. On

May 12 the bony elevation on the right mandible was enlarged and several more irregular nodules were palpated in the left supraorbital and frontal regions. The temperature had risen to 102° F., and the patient had begun to cough. There was evidence of bronchopneumonia in the right lower lobe. On May 20 the patient expired in a state of extreme emaciation.

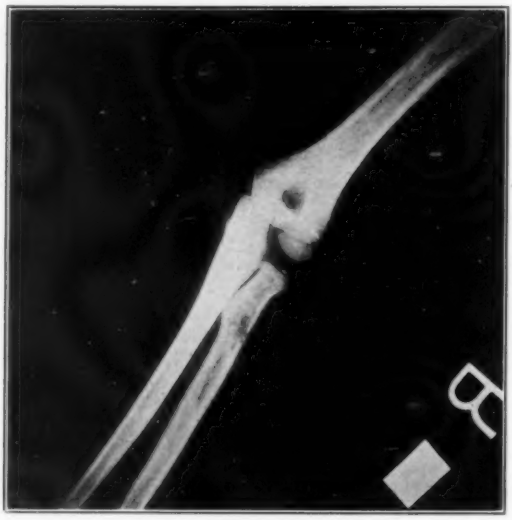

Fig. 3.—Roentgenogram of the right arm showing erosion of the shaft of the humerus and the radius below the head.

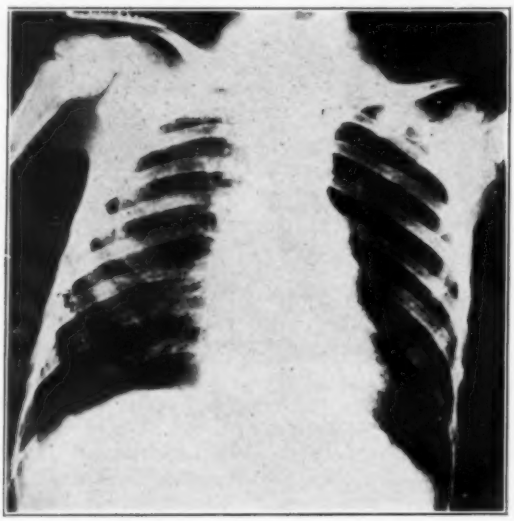

Fig. 4.—Roentgenogram of the chest showing rarefaction in the ribs, scapulae, and clavicles.

AUTOPSY REPORT

Gross Findings.—The autopsy was performed by Dr. Otto Saphir, pathologist, about four hours after death. The body was that of an underdeveloped, markedly emaciated male child about six years old. The skin showed many small nodules measuring as large as 5 mm. in diameter; they contained a large amount of yellowish creamy material. Some of these nodules showed shallow ulcerations, a few of which were covered with a reddish brown crust. The skin was very thin and there was little subcutaneous fat tissue.

The serous cavities revealed no abnormalities.

The heart showed no gross changes.

Both lungs were air-containing. The right lower lobe showed a few patches of bronchopneumonia.

The liver was larger than normal and of firm consistency. The capsule was smooth. On section, the architecture of the cut surface in many portions was obscured. Where visible, the central zones were red, depressed, and some of them fused by confluence. The periportal spaces appeared bright yellow. No tumors or leucemic infiltrations were visible grossly.

The spleen was slightly larger than normal and of firm consistency. The cut surface was reddish brown. The trabeculae were clearly visible. The follicles appeared small and indistinct.

The kidneys were enlarged and soft. The capsules stripped away with ease, leaving smooth surfaces. Throughout the surfaces, a few gray nodules were seen, measuring up to 6 mm. in diameter. On section, the architecture of the cortex was obscured. Nodules which were also visible on the cut surfaces appeared grayish and well defined. The pelves, ureters, and bladder revealed no gross abnormalities.

The pancreas and suprarenals revealed no gross changes.

The esophagus was dilated. The mucosa of the esophagus showed several small ulcers measuring 2 to 3 mm. in diameter, which were surrounded by a yellowish necrotic tissue. Throughout the stomach, duodenum, and jejunum, many nodules were encountered which measured from 3 to 12 mm. in diameter. These nodules seemed to have risen in the submucosa and many were covered by mucosa with small areas of ulcerations. The nodules were very easily movable from the underlying muscularis; they were soft, light gray, and revealed a homogeneous cut surface.

The lymph nodes throughout the body were slightly enlarged and softer than normal. On cut section, they were gray and showed a finely granular surface.

The skull was much thinner than normal and showed many depressions and lacerations (moth-eaten). Between the calvarium and the dura, a large, flat yellowish brown tumor was noted, measuring 2 to 3 mm. in thickness. The tumor extended over the convexity of the brain, completely filling the epidural space. It was firmly attached to the dura and could not be removed from the bone. The tumor did not extend into the arachnoidea or brain. The base of the skull showed no tumor growth. Both orbits contained a large amount of edematous fat tissue, but no tumor growth.

Multiple sections of the brain revealed no gross abnormalities.

The bone marrow of the sternum and ribs was grayish red. The bone marrow of the right tibia was light gray, in some portions more yellow; it was much firmer and more compact than normal and showed a finely granular cut surface.

Histologic Examination.—

Heart: Sections of the myocardium showed no changes.

Lungs: With the exception of a bronchopneumonia in the right lower lobe, no abnormalities were noted.

Liver: The liver cells showed a moderate granularity of the cytoplasm. The liver cells surrounding the central veins contained large fat globules. There was no cellular infiltration.

Spleen: The follicles appeared atrophic. There was a slight increase of connective tissue throughout the pulp. The sinusoids were distended and filled with red blood cells. A moderate number of monocytic cells were seen throughout the pulp. No accumulations of lymphocytes were found in any of the fields.

Kidneys: The lining cells of the convoluted tubules were swollen; their cytoplasm was finely granular. In many portions the nuclei were absent. Some of the sections showed large accumulations of cells with paucity of cytoplasm, but distinctly outlined, deeply stained nuclei. These cells resembled large lymphocytes. They were found in several sections, but were situated mainly in the cortex (Fig. 5). Giemsa stain revealed that only a few of these cells showed granules in their cytoplasm.

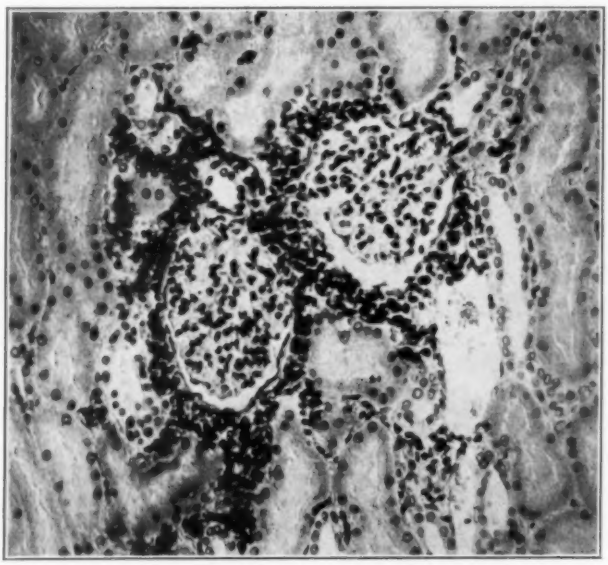

Fig. 5.—Kidney. Section through kidney cortex showing infiltration of large mononuclear cells around glomeruli and proximal convoluted tubules. Many of the cells are round, the nuclei dense, and the cytoplasm sparse resembling large lymphocytes. (×120).

Most of these granules were stained red, a few were blue. These areas of cellular infiltration corresponded with the nodules noted in the gross sections.

Suprarenals: No abnormalities were noted.

Pancreas: Throughout the pancreas very many cells, similar to those seen in the kidneys, were noted. They invaded the parenchyma in large masses, so that only outlines of pancreatic acini could be recognized. Giemsa stain showed very few granules in the cytoplasm of these cells.

Intestines: Sections of the esophagus, stomach, and small intestines revealed, in the region of the submucosa, large accumulations of cells similar to those described in the kidneys and pancreas. In a few sections there was some necrosis which had led to the formation of small ulcers. Very few polymorphonuclear leucocytes were found in these regions. The sections which were taken from the esophagus showed many such ulcers. The blood vessels in these regions showed no changes.

Lymph nodes: The architecture of the lymph nodes was preserved, the sinusoids were distended. The follicles were small and indistinctly visible. Many large lymphocytic cells, poor in cytoplasm, were found. Giemsa stain revealed no granules within the cytoplasm of these cells.

Skin nodules: Sections which were taken from the skin nodules revealed mainly necrotic tissue, a moderate number of polymorphonuclear leucocytes, and a few large lymphocytic cells similar to those described before.

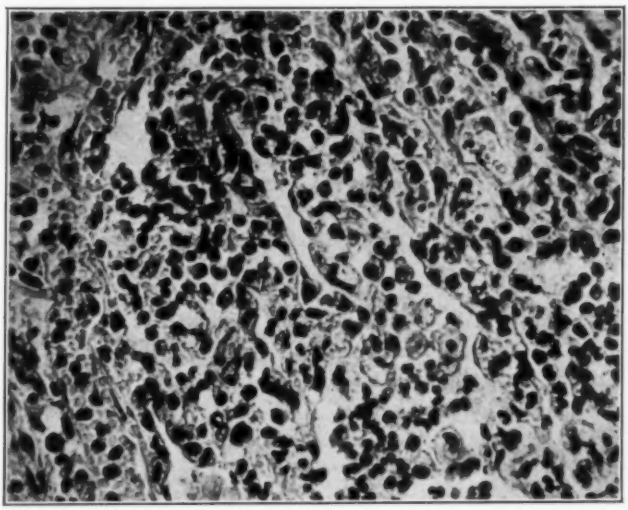

Fig. 6.—Dura. Note the marked cellular infiltration. The cells resemble those in the kidneys. Variation in size, shape, and staining quality can be seen. There are a few mitotic figures. (×380.)

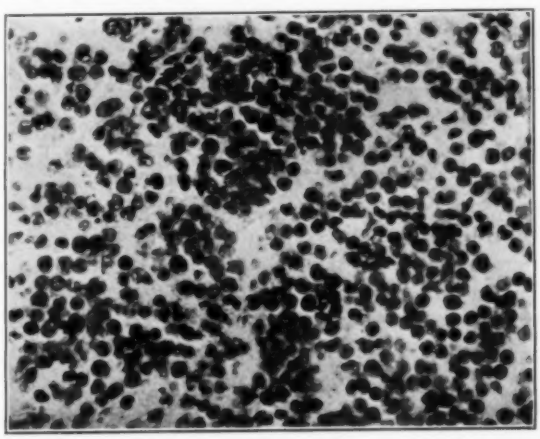

Fig. 7.—Section of bone marrow showing the presence of large cells, many resembling myelocytes. There is variation in size, shape, and staining quality. The normal marrow spaces are absent. Note the mitotic figures in the upper central field. (×500.)

Dura: Sections of the dura showed cells similar to those previously described (Fig. 6). The nuclear details were not recognizable and very little cytoplasm was present. Neither the Giemsa nor the oxydase stains revealed any granules. There were no mitotic figures. In only very few fields did the cells actually invade the deeper portions of the dura.

Brain: Sections of the brain showed no abnormal changes.

Bone marrow (tibia): In some of the fields the bone marrow showed cells similar to those described in the dura (Fig. 7). The Giemsa and oxydase stains revealed a few granules within the cytoplasm. Other sections revealed cells which were larger than those described before, which showed a loose chromatin network of the nuclei, and many mitotic figures. The cells in general varied in size, shape, and staining quality, and appeared to infiltrate the bone marrow. In many portions large areas of necrosis were seen in which only ghosts of cells were recognizable. The Giemsa and oxydase stains revealed many neutrophilic, a few eosinophilic, and basophilic granules in the larger cells. Some of the sections revealed an invasion of the bone and periosteum by these cells. Sections which were taken from the bone marrow of the ribs and sternum showed a moderate number of fat cells in addition to occasional large cells similar to those described in the dura.

DISCUSSION

The clinical and pathologic diagnosis in this case presented many difficulties. The appearance of multiple tumors in the skull, proptosis, x-ray evidence of rarefaction and destruction in the membranous and long bones, marked anemia, severe emaciation and cachexia, suggested the possibility of generalized sarcomatosis (the primary focus unknown), chloroma, multiple myeloma, sympaticoblastoma of the Hutchinson type, generalized xanthomatosis (Christian's syndrome), lymphosarcoma, atypical leucemia, and leucosarcomatosis. Because this case offered so many diagnostic possibilities, and because the anatomic and histologic findings at autopsy were so unusual, it is felt that a detailed discussion of the differential diagnosis would be of value.

Leucemia.—Clinically I did not feel that this case was one of leucemia. In infancy and childhood leucemia occurs most frequently in the acute form with a course resembling sepsis with extreme prostration and high fever, ulcerative and gangrenous lesions in the buccal mucosa, tonsils or pharynx, associated with enlargement of the lymph nodes and spleen, purpuric manifestations, and the presence of many immature lymphoid or myeloid cells in the peripheral blood. Repeated examinations of the blood in this case failed to reveal many immature cells. The superficial lymph nodes and the spleen were only slightly enlarged. Diffuse destruction of bone as was found on x-ray examination is very unusual in leucemia. Ewing[2] states that "the spongy trabeculae are often absorbed and even the shafts may be thinned, but a distinctly aggressive destruction of bone as in true tumors is missing." Postmortem findings were not typical of leucemia. The lymph nodes did not show marked hyperplasia, the splenic follicles were atrophic, and the bone marrow consisted mainly of cells that

varied in size, shape, and staining quality, many of which revealed mitotic figures, rarely seen in leucemia,[3] but common in neoplasms.

Chloroma.—This disease is essentially one of early childhood, and is characterized by the development of infiltrating tumor masses in the cranial bones, orbits, paranasal sinuses, ribs, and sternum. Painful exophthalmos, progressive blindness, and deafness commonly occur. The sclera frequently have a peculiar greenish hue, unlike icterus. The lymph nodes, liver, and spleen are frequently enlarged. The presence of tumor masses in the alimentary tract may produce severe intestinal symptoms. The blood shows immature cells, either of the lymphoid or myeloid type usually with a moderate to marked leucocytosis. At autopsy tumor masses are found most commonly involving the periosteum, the dura, and the ligamentous structures. The tumor growths in a vast majority of cases are characteristically of *greenish color*. The bone marrow is red or grayish red, occasionally greenish. Histologically, the tumor cells tend to form parallel rows, and appear as large undifferentiated nongranular mononuclear cells. My case was not typical of chloroma. From the blood findings one could not establish the presence of leucemia; a great many of the bone marrow cells exhibited malignant changes conforming to a true neoplasm. The morphologic appearance of the epidural tumor, however, easily could have suggested the diagnosis of chloroma even though it did not present the characteristic green color.

Multiple Myeloma.—Multiple myeloma is an exceedingly rare disease in childhood.[4] It is characterized by a diffuse involvement of the osseous system with predilection for the vertebra, sternum, ribs, clavicles, scapula, and ilium. Paraplegia occurs in 40 per cent of the cases, indicating extensive disease of the vertebra. A pathologic fracture is frequently the first indication of bone disease, occurring in 62 per cent of the cases and most commonly involving a rib.[5] Marked involvement of the skull may produce exophthalmos and symptoms of increased intracranial pressure. Bence-Jones' proteinuria is found in nearly 50 per cent of the cases. Berkheiser[4] states that any marked change in the blood picture speaks against myeloma. X-ray examination reveals multiple areas of medullary rarefaction with erosion of the cortex, in places presenting a definitely punched-out appearance. Perforation is frequently observed. Histologically, the tumors are composed of large cells often resembling plasma cells lying in a vascular, delicate connective tissue and stroma. Clinically, I feel that it is possible to exclude multiple myeloma. Several examinations failed to reveal Bence-Jones protein in the urine. There were no pathologic fractures, and x-ray examination in my case revealed a diffuse riddling of the bones involved, unlike multiple myeloma in which the areas of rarefaction are usually isolated and sharply defined. The

epidural tumors and cellular infiltrations in the pancreas and kidneys found at autopsy are unusual in myeloma. Histologically, the tumor cells do not resemble the large plasma cell type usually found in myeloma.

Sympaticoblastoma.—Sympaticoblastoma of the Hutchinson type is characterized in the majority of cases by swelling of the bones of the skull, exophthalmos, unilateral or bilateral with ecchymotic discoloration of the lids, profound secondary anemia without leucocytosis and the presence of an abdominal tumor in 50 per cent of the cases. Increased intracranial pressure with progressive blindness is common. The tumors in the cranial bones increase rapidly in size filling up the temporal fossae, and proptosis becomes so marked that the cornea ulcerates. The superficial lymph nodes are moderately enlarged. X-ray examination reveals a diffuse mottling of the skull, periosteal thickening of the long bones, and small areas of destruction. At autopsy a primary tumor is found, usually in an adrenal gland. Histologically, the tumor is composed of cells and their processes, derived from embryonic sympathetic nervous tissue. An abdominal tumor was not palpated in my case. Postmortem examination obviously revealed that we were not dealing with a sympaticoblastoma.

Lymphosarcoma.—Lymphosarcoma occurs with greatest frequency between the ages of twenty and twenty-five years, and rarely in childhood.[2] It arises in the retroperitoneal, mesenteric, mediastinal, cervical, and superficial lymph nodes, and uncommonly in isolated nodes in the intestinal wall. Kundrat[6] states that it is a regional disease of lymphoid tissue which spreads as a continuous growth through the lymph channels, thereby differing from the systemic character of leucemia. Isolated metastases in distant organs are rare, but in advanced cases the growth may invade the blood vessels, and true metastatic tumors form in the lungs, kidneys, skin, and other organs. In such instances atypical cells similar to those found in the tumor may also appear in the peripheral blood in large numbers, making the distinction between lymphosarcoma and leucemia difficult. A primary growth in the lymph nodes or lymphadenoid tissue could not be demonstrated in my case; the invasive and locally destructive characters of lymphosarcoma were absent in the organs involved, infiltration and accumulations of abnormal cells being the distinctive features. Also, anaplasia and mitosis of the cells were conspicuously absent in the lymph nodes described.

Xanthomatosis (Christian's syndrome).—In 1919 Christian[7] described a clinical syndrome in children consisting of "Defects in Membranous Bones, Exophthalmos and Diabetes Insipidus." He considered a disturbed pituitary function as the cause of the syndrome. Rowland[8] in 1928 associated Christian's syndrome with generalized xanthomato-

sis, a disease primarily the result of disordered fat metabolism in which the reticulo-endothelial system shows an excessive storage of lipoids, frequently in the form of cholesterol. The disturbed pituitary function is due to the encroachment of pseudotumors upon the pituitary body or tuber cinereum. Orbital involvement frequently causes exophthalmos. The most outstanding clinical feature is the presence of defects in the skull characteristically involving the inner table of the skull more than the outer, having distinct, clear-cut but irregular edges, and often presenting a maplike or geographical appearance (Schüller). There is a tendency of the disease to spontaneous remissions and healing with new bone formation following x-ray treatment to the affected areas.[9, 10, 11] My patient showed no evidence of disturbed pituitary function, the course of the disease was progressive, x-ray examination of the skull did not reveal distinct, clear-cut areas with irregular edges, and x-ray treatment of the affected regions did not result in healing. Two examinations of the blood revealed normal cholesterol values, and postmortem histologic examination did not reveal the typical lipoid laden xanthoma cells.

Leucosarcomatosis.—In 1904 Sternberg[12] attempted to isolate from recognized cases of leucemia certain cases characterized by the presence in the blood of large mononuclear cells which he believed to be pathologic lymphocytes, arising from an original tumor, and by means of true metastasis, producing a generalized systemic disease. He applied the name leucosarcomatosis and called these cells "leucosarcoma cells." Anatomically this condition differed from typical leucemias in a more marked invasion into the lymphoid tissues, particularly the mediastinum, with tumor formations—a true blastomatous condition as opposed to a hyperplastic condition which he believed characteristic of the true leucemias. Within recent years the common belief is that the large mononuclear cells in the blood are myeloblasts or undifferentiated stem cells and that leucosarcomatosis is more closely related to myeloid than to lymphoid leucemia.

In 3 of Sternberg's original 6 cases, a sarcomatous tumor was found in the mediastinum. Two cases exhibited tumor formation on the inner surface of the dura and in the skull. The spleen was enlarged in 5 cases and there was generalized enlargement of the lymph nodes in 2 cases. In 1915, eleven years later, Sternberg[13] reported a case of leucosarcomatosis which clinically resembles my case:

> An eleven-year-old child complained of fatigue and difficulty in breathing of five months' duration. Examination of the blood revealed a white blood count of 31,000 on admission and 5,250 shortly before death. Many large mononuclear cells, "leucosarcoma cells," were observed at various times which led to the diagnosis of a probable leucosarcomatosis.

W.B.C. 31,000 to 5,250; lymphocytes 4 to 28 per cent; polymorphonuclear leucocytes 5 to 30 per cent; myelocytes 4 to 9 per cent; "leucosarcoma cells" 42 to 85 per cent.

Postmortem examination revealed large, flat, firm tumors on the inner surface of the dura; enlargement of the spleen, liver, mediastinal mesenteric and retroperitoneal lymph nodes some of which were fused by confluence. The tumors of the dura consisted histologically, of large mononuclear cells similar to those found in the blood. The cells invaded the dura. Similar cells were found in large numbers in some of the lymph nodes and invaded the surrounding fat tissue. They were also present in the splenic pulp, in the interlobular spaces of the liver, and in the bone marrow.

It is true that some of the large mononuclear cells that were observed in the blood of my case and classified as lymphocytes, might possibly have been "leucosarcoma cells." Sternberg describes the tumor cells as being similar to those found in the blood. It is also possible that the abnormal cells in my case were identical with those found in the epidural tumor. In Sternberg's case the tumors showed a marked predilection for the lymph nodes and lymphatic tissues; mine was conspicuous for the paucity of lymphatic tissue invasion.

Realizing that it is at least not a clear case of leucosarcomatosis, a further search of the literature was made in an attempt to classify my case. This search revealed only one case, similar enough to warrant my using the classification presented therein.

In 1912, Buschke and Hirschfeld[14] reported a case of a twenty-two-year-old woman who, following a tuberculin injection, developed many tumor nodules throughout the skin. The blood picture was normal until four days before death when the white blood count rose from 11,000 to 33,000 and many peculiar "tumor cells" appeared in the blood. A puncture of the skin tumors revealed similar cells. The cells were large, the nuclei round, sometimes indented, and showed a dense chromatin network and often several nucleoli. The cytoplasm was stained sky-blue (Giemsa). In some of the cells azure granules could be found in varying numbers. A differential count at that time revealed polymorphonuclear leucocytes 35 per cent, small lymphocytes 23 per cent, large lymphocytes 8 per cent, large mononuclear cells 5 per cent, and "tumor cells" 25 per cent. Clinically, this was thought to be a form of leucemia consisting of abnormal cells classified by Pappenheim as "lymphoidocytes." The autopsy revealed in addition to a bilateral pulmonary tuberculosis, tumor nodules throughout the skin, some of which were the size of a walnut. The eyes were somewhat bulging, the lids swollen. The bones showed reddish gray tumor masses. The mucosa of the stomach presented tumor-like red excrescences. The large and small intestines showed ulcer-like depressions. Both ovaries and parametria were invaded by tumors. The lymph nodes surrounding the abdominal aorta were enlarged, firm, and infiltrated by tumors. When the scalp was removed, tumor nod-

ules could be demonstrated throughout the frontal region. The dura also was covered by firm tumor nodules throughout. Smears taken from the various organs revealed cells which were identified as lymphoidocytes. In the lymph nodes many mast cells were found. Many mitotic figures could be demonstrated. The skin tumors showed large mononuclear cells similar to those found in the blood.

In discussing their case, Buschke and Hirschfeld state that there is no question that it is one of sarcomatosis. The primary tumor could not be located with certainty. They mention that in the literature there are cases of lymphosarcomatosis in which evidence of lymphatic leucemia is also present. They excluded this disease because they were unable to discover a new growth originating in the lymphatic organs. In their own case the tumors in the lymph nodes and spleen were relatively insignificant and were most marked in the bone marrow, skin, and ovaries, a pronounced deviation from the usual findings in lymphosarcoma. They considered as a second possibility leucosarcomatosis. The lymphoidocytes they described were not similar to Sternberg's "leucosarcoma cells"; nevertheless, they were inclined to designate their case leucosarcomatosis in the sense that all leucemic proliferations, whether originating in myeloid or lymphatic hematopoietic organs, exhibiting a definite tendency toward an anatomically malignant growth of myeloid or lymphadenoid tissue should be called leucosarcomatosis. In summarizing their discussion they specify that theirs is the first case of leucosarcomatosis to be reported in which the new growth originated in the myeloid hematopoietic system and therefore proposed to classify it as one of "myelosarcomatosis." Several years later, Hirschfeld,[15] in discussing this same case states that the lymphoidocytes described were of myeloid origin and the skin tumors consisted of dedifferentiated myeloid tissue.

An analysis of my case brings out a striking similarity clinically and anatomically to Buschke and Hirschfeld's case of myelosarcomatosis. In both cases the white blood counts were only slightly elevated and the stained smears showed many atypical cells which resembled young lymphocytes. Hirschfeld is recently of the opinion that they are dedifferentiated myeloid cells. My case also exhibited nodules throughout the skin, many of which had undergone abscess formation; however, at autopsy many mononuclear cells were present resembling those found in sections of tumor nodules in other organs. Similarly, tumors were present in the bones, gastrointestinal tract, and in the dura mater, consisting of cells many of which were myeloid in character. Both cases were conspicuous for slight lymphatic involvement. In many places the malignant nature of the growths was made evident by the presence of mitotic figures and invasion of surrounding structures.

SUMMARY

1. A case of an extremely rare disease in a child six and a half years old is presented in which the essential features are multiple malignant tumors throughout the skeletal system, gastrointestinal tract, kidneys, pancreas, and dura mater which histologically have the appearance of undifferentiated myeloid tissue. The blood revealed many atypical cells that resembled young lymphocytes but may have been myeloid in origin.

2. In an attempt to classify this case, a detailed clinical and pathologic differential diagnosis is presented.

3. Emphasis is placed upon the difficulty in separating certain cases of leucemia from neoplastic disease.

4. With a great deal of reservation I have classified this case myelosarcomatosis after Buschke and Hirschfeld.

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HYPERTROPHIC PYLORIC STENOSIS IN TWINS

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LASCH,[1] in discussing the etiology of hypertrophic pyloric stenosis, suggested the study of its occurrence in twins as a likely means of determining, at least in some cases, whether this condition is congenital. He reported a case in one of monozygotic twin girls and from this concluded that it was probably not congenital. He suggested, however, that a greater number of cases must be recorded before a definite opinion could be formed. One must be very cautious in concluding that this is not hereditary but environmental as monozygotic twins might be hereditarily different, due to an unusual splitting of the ovum giving rise to great variability in the anlage. This view is not generally accepted, however. Lasch's twins were physically identical and the placenta had but one corium. Single corium, while exceptional, may also be found with dizygotic twinning though Lasch did not think the possibility of dizygotic twins applied to the case he reported. His patient died a few days after operation, while the twin sister at no time showed symptoms or signs of pyloric stenosis.

Recent studies of mental disorders in twins by Rosanoff[2] should throw considerable light on the etiology of these conditions as regards heredity and environment. This method of clinical investigation also lends itself to the study of physical disorders and particularly pyloric stenosis, as Lasch has pointed out.

The comparative rarity of this condition, together with the fact that obstetricians report that approximately one birth out of 80 is multiple, makes the possible number of cases small. It is difficult to determine from some reports whether the twins are monozygotic or dizygotic. Wherever possible, this has been investigated by correspondence.

All the reported cases discoverable, were reviewed with the hope that interest would be created in reporting diseases occurring in monozygotic and dizygotic twins. In time a sufficient number may be recorded to make some conclusions possible on this and other conditions.

Redalin mentioned pyloric stenosis in two sets of twins, but said nothing about the type of twinning, so his cases cannot be used.

Davis,[3] in 1924, reported pyloric stenosis in twin boys, but unfortunately the records do not show whether the twins were monozygotic or dizygotic. (Personal communication.) The diagnosis was confirmed by operation and both patients made uneventful recoveries.

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Moore's[4] cases also occurred in monozygotic twin boys. (Personal communication.) They were not seen until the fourth week after onset, at which time their condition was precarious as well as complicated by malaria. Both presented typical signs and symptoms of pyloric stenosis, diagnosis being confirmed at operation. Due to their poor condition both died about a week after operation.

Bilderback's[5] twins were monozygotic (personal communication), two months premature males. Typical tumors were found at operation. One twin died while the other made an uneventful recovery.

Monrad[6] reported 228 cases of hypertrophic pyloric stenosis of which three cases were in three pairs of twins. The type of twinning was not mentioned but since they were normal one would suspect them to be dizygotic even though Lasch did not find it so in his cases.

Because of the discussion as to identification of monozygotic twins, the following criteria were used to establish this in our cases:

(1) Both were males, identical in every way by physical examination except one was more emaciated due to earlier onset of symptoms;

(2) Hand prints were taken and found sufficiently alike to be classified as "1 Absolute Ab. 1" according to Reichle.[7]

(3) For additional proof the obstetrician's note at time of delivery is quoted: "The placenta was a large one in size although it was not weighed. Each cord was inserted at opposite sides of the placenta, each one having a battledore attachment. There was only one chorion present. The amnion separated two amniotic sacs. No line suggestive of a fusion of two placentas could be found. It was apparently composed of only one placenta, and in every way appeared normal."

CASE REPORTS

CASE 1.—*History.*—T. K., aged nine weeks, was admitted to the University of California Hospital, February 9, 1931, with the chief complaint of vomiting since one month of age. Family history was significant as mother had arrested pulmonary tuberculosis and the twin brother had also been vomiting although not so much. Delivery had been by low forceps, birth weight 6 pounds, with question of prematurity. No breast milk was available and he was given whole cow's milk, boiled, diluted with water. After a week this was changed to Dryco upon which he did well for three weeks then started vomiting. Formula was again changed to lactic acid milk, next to diluted evaporated milk and later to Eagle Brand milk without improvement. For one week before entry he was given atropine 1/1000 to 1/600 grain before feedings. The vomiting continued, occurring shortly after feedings and at times was projectile. For two days previous to admission the vomitus contained material resembling coffee grounds and he vomited water as well as milk. Intramuscular blood (15 c.c.) was given. Marked constipation had been noted for two weeks although enemas showed some return. There had been no infection.

Weight on admission was 3170 grams and patient was markedly dehydrated, emaciated and pale having the typical appearance of a "little old man" with very thin cheeks and sunken fontanel. He seemed very hungry and sucked his fists con-

stantly. Skin was pale, dry and inelastic and there were small shotty glands in the cervical and axillary regions. Chest was poorly clothed but otherwise negative. Abdomen was scaphoid, thin and a small firm tumor mass could be felt in the right upper quadrant. No peristaltic waves could be made out at any time.

Laboratory Data.—Blood on admission was Hemoglobin 82 per cent (Sahli), R.B.C. 6,110,000, W.B.C. 18,800. Diff.: Polys. 52, Lymphocytes 45, Mononuclear 1, Basophiles 1, Myelocytes 1. Blood chemistry: Plasma CO_2 = 64.3 volumes per cent, Plasma Cl = 479 mg. per 100 c.c. N.P.N. = 27.3 mg. per 100 c.c. Wassermann and Tuberculin 0.1 were both negative.

Barium meal with fluoroscopy showed 80 per cent gastric retention at the end of 6 hours. Bronchopneumonia was revealed in the permanent films made.

Fig. 1.—T. K. left; D. K. right. Aged twenty-one months.

Treatment.—Patient was given parenteral fluids and thickened feedings preceded by phenobarbital 0.004 gram. Projectile vomiting of water and formula continued and gastric lavage consistently showed marked retention of food in the stomach.

After further preparation with parenteral fluids a Rammstedt operation was done on February 10, 1932. A typical pyloric tumor was found. Just before closing the abdomen the peritoneal cavity was filled with normal saline.

After operation, the infant retained the first few small feedings of whole lactic acid milk with added Karo sugar, but then began to vomit. Vomitus contained old blood. His temperature was 38.6° C. He coughed occasionally but his chest was negative to physical examination. He continued to vomit most of his feedings and the amount of blood increased so that the second postoperative day he ap-

peared very pale and decidedly worse. His hemoglobin was 34 per cent (S) R.B.C. 1,780,000. He was given 75 c.c. citrated blood with great difficulty, presumably due to an anomaly of the valves in his veins. Following this transfusion he improved generally, vomited less but his stools became dark and tarry. His hemoglobin was 42 per cent (S) and R.B.C. 2,480,000.

Two days later he was transfused again with the same difficulty. Parenteral fluids were administered as needed. After a third transfusion his hemoglobin went up to 65 per cent (S) and his R.B.C. were 3,700,000.

After five days vomiting ceased and the small amounts he spit up did not contain blood although his stools continued to be tarry for a few days longer and a positive Benzidine test was obtained for a still longer period, but finally the stools became normal. He gained slowly and additional transfusions were necessary.

On April 6 he had fever and signs of bronchopneumonia were present, most marked on the right. This was confirmed by roentgenogram. The following day the left ear drum was incised and drained pus for a few days. His cough and a low-grade fever persisted. Chest films remained unchanged and suggested perifocal tuberculosis. Tuberculin test 1.0 mg. which was repeated, was negative.

Since his weight had become stationary the formula was changed to two parts evaporated milk to one part of stock solution, following which he gained steadily in spite of occasional vomiting.

On March 26 he developed definite signs of whooping cough after an accidental exposure some days before. He became extremely ill, cyanotic and toxic and vomited constantly. He was given pertussis vaccine without demonstrable improvement. He improved when placed in an oxygen tent but became cyanotic whenever removed for feedings. After a very stormy course he was discharged from the hospital on June 29, 1931, still having a slight cough but afebrile and otherwise in good condition. Discharge weight 5800 grams.

Case 2.—*History.*—D. K., white male, aged nine weeks, was admitted to the University of California Hospital on February 10, 1931, with the same complaint as his brother, who had been admitted the previous day, vomiting since one month of age only less severe. Birth and feeding history were practically the same as that of twin brother. He did well for a month when he began to vomit a small amount of formula. This usually occurred immediately after feeding, never longer than one-half hour. Vomiting was projectile in type and did not show mucus, blood and bile. Vomiting continued intermittently for two weeks during which he lost most of his feedings, so the formula was changed to evaporated milk 6½ ounces, water 14 ounces, 4 ounces every four hours, with cessation of vomiting until two days before admission. During this final period he vomited practically everything including water. He had gained 3 ounces since birth but failed considerably during the past three weeks. Stools had been few and constipated and there had been no infection or fever.

Physical examination on admission revealed a well-developed but poorly nourished dehydrated infant, weighing 3800 grams. His skin was inelastic, dry and pale. He had a soft scaphoid abdomen, and a definite small firm mass could be felt in the left upper quadrant but no peristaltic wave could be made out.

Laboratory Data.—Hemoglobin 63.7 per cent (S), R.B.C. 3,150,000, W.B.C. 10,900, Polys. 32 per cent. Tuberculin negative. Plasma CO_2 43.7 volume per cent. Barium meal under fluoroscopy showed marked retention.

Treatment.—For three days following admission whole lactic acid milk with 10 per cent added Karo thickened with rice flour, was given every four hours with phenobarbital 0.004 twenty minutes before each feeding. Additional fluids were administered parenterally. Vomiting continued and soon became dark red with

blood and a markedly positive benzidine test for blood was also noted in the few stools passed. Gastric lavage, twice daily, consistently showed considerable retention. February 13, a Rammstedt operation was done under local anesthesia and a typical olive-shaped tumor was found. A small section taken for examination revealed hypertrophy, hyperplasia, interstitial edema and hyalinization of pyloric smooth muscle. Just before closure of the wound the abdomen was filled with normal saline. His postoperative course was uneventful. He took gradually increasing amounts of formula without vomiting and his weight steadily increased. His stools later became negative for blood. He was transfused to improve his anemia but as in the case of his brother, this was difficult because of an apparent anomaly in the valves of his veins.

Patient was discharged 15 days after operation weighing 4380 grams, a gain of 580 grams since admission, and continued to do well.

Both patients were seen again in September, 1932, aged 21 months. They had been perfectly well since discharge. T. K. weighed 31 pounds 10 ounces and was 34¼ inches tall, while D. K.'s weight was 30 pounds 7 ounces and his height 34½ inches. T. K. has been five months behind his twin in development, that is, walking, talking, etc.

CONCLUSIONS

1. Hypertrophic pyloric stenosis is reported in monozygotic twin boys. A review of previous reports shows that accurate information regarding monozygotic or dizygotic twinning is seldom mentioned, decreasing the value of these reports. Reports of pyloric stenosis occurring in only one of twins should likewise be carefully reported regarding placentation.

2. Hypertrophic pyloric stenosis in twins is rare and in the small number collected one would conclude that there is more evidence in favor of a congenital theory than against it, but one must await the recording of more cases before a real conclusion can be made.

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HYPERTELORISM

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WE WISH to report two cases of hypertelorism. It is our opinion that this condition is more frequent than one would infer from a review of the small number of cases described in the English literature.

The standard American pediatric texts in most instances do not refer to this subject. Williamson[1] refers briefly to hypertelorism, saying: "This title has been introduced by Greig to describe a group of cases which is characterized by widespread separation of the eyes as the result of defective development of the sphenoid bone. Mild degrees of the condition are common and these give rise to no symptoms, but in marked cases there may be monocular vision and mental deficiency of extreme degree."

It is also referred to in *Diseases of Children* by Garrod.[2]

It was first described and named by Grieg,[3] of Edinburgh, who observed two cases over a period of several years, and made an exhaustive study of the macerated skull of his first case. He states that the enormous breadth of the anterior nares is the most striking feature of the skull (the opening being quadrilateral instead of pyriform), and that the skull shows the small size of the great wings of the sphenoid with a disproportionate largeness of the small wings.

Etiology.—"That part of the sphenoid developed in cartilage (the lesser wings) early develops into bone—about the third month of fetal life; . . . The lesser wings . . . increase greatly in width . . . outdistancing the greater wings; thus, the orbits retain the fetal lateral deviation, because they are fixed . . . due to the premature ossification in the sphenoid."[3]

The salient feature observed during life is the widespread separation of the eyes, and the term ocular hypertelorism coined by Grieg accurately describes this feature.

While most of the recorded cases come from the British Isles, Reilly,[4] of San Francisco, in an excellent article reported the fourteenth, fifteenth, sixteenth, and seventeenth cases.

Diagnosis.—This is usually easy since it is only in this condition that we find the marked distance between the orbits. The condition is readily recognized at birth. The face appears small, the cranium large, the nose has a broad bridge and is generally retroussé. The eyes are

set far apart with their horizontal axes directed laterally and strabismus is often present. While the height and circumference are usually normal, the skull length is shortened and the occiput flat, giving a brachycephalic type.

Physical development may be normal or retarded. Mental deficiency may or may not be present, and other deformities may be found, such as syndactylism, high palate, undescended testes, and acrocyanosis.

X-ray of the skull shows the wide separation of the orbits and large anterior nares. Intersutural bones may be present or the sutures incomplete with absence of digitations.

Fig. 1.—Case 1.

Fig. 2.—Case 2.

According to Reilly, the most common form is that with facies and a family tendency, our cases falling into this variety.

We are describing briefly two cases, a female twelve years of age and a male of six years, brother and sister. The mother of these children, aged forty years, has the typical hyperteloric facies more marked than the daughter or son. She appeared very sensitive about her condition and would not consent to allow us a picture of herself, although she showed us a picture, taken in her infancy which illustrates the facies quite well. On further question it was found that her father also had a similar appearance. As near as we could determine the mentality of both adults was apparently normal. A third child, the oldest in the family, is the only normal one.

CASE REPORTS

CASE 1.—Ed. D., male, six years of age, was brought to the physician because of frequent sore throat and head colds.

The history of birth and development appeared entirely normal, and his general health was excellent.

On casual inspection, attention was immediately drawn to the eyes which appeared to be wide spread, and the mother volunteered that the boy had been that way since birth and that her second child, a girl, had the same type of face.

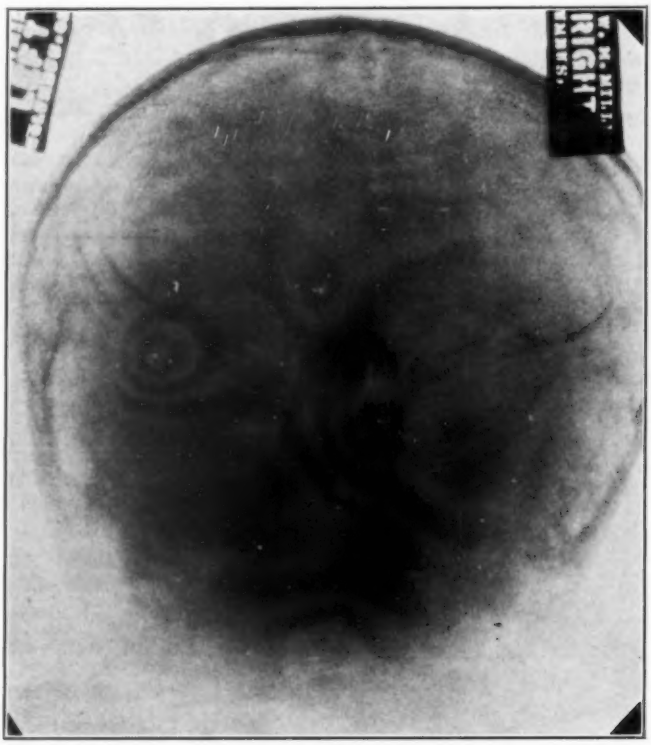

Fig. 3.—Case 2.

The essential findings are in the face and head. The skull seemed unusually large, particularly in width, the occiput rather flat, the forehead high, while the frontal and orbital prominences were very slight. It would seem that the skull has been flattened from before backward.

The other notable feature was the appearance of the eyes, seemingly far apart. The bridge of the nose was moderately depressed and broad, the nose not being retroussé.

The eyegrounds were normal and no definite strabismus was noted. The hard palate seemed high and the child spoke with a mild defect in articulation.

Physically and mentally, the child appeared to be normal in all other respects.

Tuberculin and Wassermann tests were both negative.

While this child is a mild case and the picture is not particularly convincing, the facies was characteristic on actual inspection, and served to discover the more definite case in the sister and also bring to light the definite familial history in the parent and grandparent. X-ray of the skull was not unusual.

CASE 2.—Em. D., a sister, twelve years of age, presented a more definite facies than her brother.

Her birth, developmental, and past medical histories were all quite normal. She appeared unusually alert and intelligent and was quite sensitive about her face.

The eyes were unusually far apart. The bridge of the nose was greatly depressed and broadened, while the nose was retroussé. The face seemed small in comparison to the cranium.

There were no other abnormal physical findings.

Table I gives measurements in millimeters of patients and comparison with normal subjects of the same ages.

TABLE I

ORBIT	ED. D. PATIENT	6 YR. NORMAL	EM. D. PATIENT	12 YR. NORMAL
Between internal canthi	35 mm.	30 mm.	45 mm.	24 mm.
Between external canthi	105 mm.	85 mm.	105 mm.	90 mm.
Between center of pupils	60 mm.	--	70 mm.	--
Right orbital height	30 mm.	22 mm.	28 mm.	25 mm.
Left orbital height	30 mm.	22 mm.	28 mm.	25 mm.
Right orbital width	40 mm.	30 mm.	45 mm.	35 mm.
Left orbital width	40 mm.	30 mm.	45 mm.	35 mm.
SKULL				
Greatest circumference	415 mm.	500 mm.	543 mm.	525 mm.
Greatest length	170 mm.	170 mm.	170 mm.	170 mm.
Greatest width	140 mm.	130 mm.	160 mm.	140 mm.
Cephalic index	82.3 mm.	76 mm.	94.1 mm.	80 mm.

(The cephalic index is obtained by multiplying the cranial breadth by 100 and dividing by the cranial length.)

The following is the radiologic diagnosis of the x-ray of Em. D. (Dr. W. H. Miller.)

Skull: X-ray examination of the skull made in the lateral and anteroposterior views shows an overgrowth of the lesser wings of the sphenoids which have ossified early and grew excessively. The orbits are widely separated due to the overgrowth of the wings of the sphenoids. The anterior portion of the skull is irregular in outline; suture lines are normal.

Teeth: Normal.

Sinuses: Normal.

Sella Turcica: Slightly enlarged.

SUMMARY

Two cases of hypertelorism with a definite familial history, all without mental deficiency, are reported.

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BRUCELLA ABORTUS INFECTION IN EARLY INFANCY

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ALTHOUGH a large number of reports of *Brucella abortus* infection of bovine origin in man have appeared in the literature of the last few years, reports of cases in early infancy have been conspicuous by their absence.

In a recent review of the literature Hubbard[1] cites one case from England occurring in a twenty-months-old infant and another in a male infant one year old. Mention is also made of a case in a twenty-two-months-old infant.

Hill and Monger[2] report a case in a six-and-one-half-month-old infant on breast milk and pasteurized milk, with fever, loss of weight, leucocytosis, and a positive agglutination test 1:640. This patient improved rapidly following injection of whole blood intramuscularly and the entire duration of illness was six weeks. The mother gave a history of repeated abortions.

Dietrich and Bonynge,[3] reporting 5 cases in children, including one in a one-year-old infant, list the following theories as to the cause of the infrequency of this disease in children:

1. Lack of contact with infected animals.

2. Low pathogenicity of bovine variety of *B. abortus* for man, especially when ingested; generally small number of organisms being ingested.

3. Biologic immaturity of the tissues of the younger child.

CASE REPORT

Baby G. M., male, nine months old, was admitted to the hospital January 10, 1933, with complaints of fever and restlessness. The parents were intelligent and the infant had been constantly under a physician's care. He had been breast fed until six months of age, cereals and vegetables being added to the diet in the fourth and fifth months. At six months of age he was put on a special baby brand milk from a reputable dairy; the parents were under the impression that this milk was from a single cow and was pasteurized. He had received no meats nor had he been in contact with any domestic animals. On December 17, three and one-half weeks prior to admission, the baby was seen with fever, irritability, and mucous stools which it had had for one week. At that time a bilateral otitis media was the

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only positive finding and myringotomy revealed the presence of thick pus in both ears. No smear or culture was made of this pus. There was no history of even the slightest coryza nor any symptoms referable to the ears. Two days later the baby was again seen, at which time it had a temperature of 100.5° F., was irritable and pulling at the eyes and mouth. The conjunctivae were injected and the ears were draining. The stools were loose and contained mucus but no pus or blood. The ears drained for one week and the child seemed better, but the fever and other symptoms persisted to a lesser extent.

The patient was again seen on the day of admission, at which time the temperature was 104.6° and hospitalization was advised. A detailed history revealed the following salient facts: He was perfectly well while breast fed; on November 1, when the infant was just seven months old and had been on the bottle for one month, the mother noticed that he was febrile, restless, and suffering with an excess of gas, these symptoms not being relieved by numerous changes in the formula. Fever at first was variable, often being 103° F. in the afternoon and then absent for several days; in the last several weeks it had been more constant, usually ranging from 100° to 101° F. After the first few weeks heavy sweats occurred during sleep, day and night. Appetite had always been good and there was no vomiting, but the baby seemed to have frequent abdominal cramps and the stools contained mucus at times. For about six weeks sleeplessness had been a disturbing symptom. Before the myringotomy, the baby was considered to have only an intestinal disturbance. For several days prior to admission a dry, persistent cough was troublesome. There had been no urinary or meningeal symptoms and no rash at any time during the illness. In spite of his illness the baby gained one-half pound in the month before admission.

Physical examination revealed a well-developed and well-nourished white male infant, nine months of age, very irritable and febrile. The skin was pale and somewhat muddy in appearance; there was no rash and no jaundice; the mucous membranes were slightly pale. The fontanel was almost closed and not tense or bulging. Eye, ear, nose, and throat examinations were negative. There was no mastoid swelling or tenderness. Heart and lungs were normal. The abdomen was not tender or distended; the liver and spleen were not palpable. There was no adenopathy, the extremities and reflexes were normal.

Laboratory Data.—The urine was normal on several examinations. The hemoglobin was 65 per cent (Talqvist); red blood cells, 3,690,000 per c.mm.; white blood cells, 7,800 per c.mm. Differential count: polymorphonuclears, 35 per cent; lymphocytes, 47 per cent; large mononuclears, 17 per cent, and basophiles 1 per cent. The Mantoux reaction was negative with 0.1 mg. The chest and mastoids were negative by x-ray examination.

After five days' observation, a tentative diagnosis of *B. abortus* infection was made, the progress note reading as follows: "The history of an irregular fever for two and a half months, the negative physical examination, the profuse sweats when asleep and the leucopenia tend to the belief that this is a *B. abortus* infection." A blood culture taken two days later revealed a growth characteristic of the *B. abortus-melitensis* group. An agglutination test was positive for *B. abortus* 1:180. Urine culture was negative. Culture of a milk sample was also negative but this is considered an unsatisfactory procedure.

Course in Hospital.—On admission the baby was placed on an evaporated milk formula and a normal diet for his age. In twenty-four hours the temperature had dropped from 104.6° to 98° F. It then rose to 101.8° and ranged between 101° and 102° for several days. It began to subside gradually and reached normal on the tenth hospital day and remained normal. Profuse sweats while asleep, whether day or night, restlessness, and a dry cough were the outstanding symptoms

in the first few days. These began to disappear and by the time the temperature was normal he was symptom-free, except for an occasional sweat. There was no change in his weight during his hospitalization. He was discharged symptom-free after two weeks' stay in the hospital and at the end of three months is apparently well. The duration of symptoms was eleven weeks.

Epidemiologic Study.—After the confirmatory evidence afforded by laboratory work, we attempted to investigate the milk supply. The milk was obtained from a special herd which gave no history of abortions. The milk was not pasteurized and the dairyman had forgotten to tell the mother to boil the milk, as was his custom when babies were started on this brand. The milk was not labeled as pasteurized. Blood studies in this herd revealed a number of positive and suspicious reactors.

SUMMARY

1. A case of *B. abortus* infection, beginning in a seven-months-old infant is reported.

2. This is the first case to our knowledge that has been reported from this section of the country in infancy or childhood.

3. A clinical diagnosis was made and was verified by positive blood culture and agglutination test.

4. *B. abortus* infection in infancy may be more frequent than is now recognized. Any unexplained fever should suggest the possibility of its occurrence.

5. Universal use of pasteurized milk will eliminate this disease in the early years of life.

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ALLERGIC EPILEPSY

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IDIOPATHIC epilepsy is a clinical syndrome which is as yet not clearly understood. The observation of an asthmatic child suffering from epileptic seizures brought up the question of allergy in relation to epilepsy. Spangler[1] studied 100 consecutive cases of adult epilepsy and found that in 88 per cent there was a history of allergy in the ancestors. He notes that gastrointestinal allergy is an important factor in the development of convulsions in the epileptic child. In his series Spangler reported that 32 per cent of the patients had convulsions in infancy. Among the parents and grandparents he found 11 cases of epilepsy, 35 cases of asthma, 7 of hay fever, 14 with urticaria, 6 with a history of eczema, and 6 who had migraine. Multiple allergic manifestations were observed in one-third of all the epileptic patients.

A. H. Rowe[2] states that allergy is undoubtedly the cause of certain cases of epilepsy, especially in children. He reports two such cases: (1) a four-year-old asthmatic child who was sensitive to pollens and in whom immunization resulted in freedom from asthma and cure of the epilepsy; and (2) an eleven-year-old child who suffered from petit mal for six years and was sensitive to cat, horse, and rabbit hair. Desensitization to horse hair and removal of her hair mattress resulted in complete relief for two years. S. J. Levin[3] reported a three-year-old child with epileptic seizures in association with sensitization to American, Swiss, and Roquefort cheese. On eliminating cheese from the diet there was a complete cessation of epileptic reactions. Levin gives credit to Pagniez and Lieutaud[4] for having first pointed out the frequent occurrence of allergic manifestations in certain instances of epilepsy. Their first report was that of a young man who suffered from epileptic seizures which were induced by eating chocolate.

In this country J. L. Miller[5] was among the first to emphasize the importance of allergy in relation to the epileptic syndrome. He expresses the opinion that the epileptic seizure is an anaphylactic manifestation, and thinks that in some cases of epilepsy food sensitization is responsible.

Angiospasm is an important factor in the explanation of epileptic manifestations, and is regarded by some as one of the effects of allergy. There are a number of authorities who explain the epileptic syndrome on the basis of a cortical ischemia induced by angiospasm. (Perez, Olkan, Bolsi, Etienne.)

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Back of these allergic and epileptic manifestations there is some hereditary defect which is transmitted by the germ plasm. Thus Frugoni[6] has proved that the allergic constitution is transmissible through either parent, although the type of manifestations may differ in parent and child.

As to the nature of this metabolic or constitutional defect, little is definitely known. However, Auguste Lumiere[7] in 1921 published a brilliant hypothesis in his study on the rôle of colloids in biology. This work deserves to receive more attention since it is based on experimental evidence and seems of great practical importance. Lumiere maintains that anaphylactic phenomena are due to an alteration in the colloids of the tissue fluids and blood plasma wherein the usually finely dispersed colloid particles are agglutinated and form precipitates in the perivascular lymphatics and tissue spaces. A flocculation of these altered colloid particles in the lungs causes asthmatic symptoms; in the brain it results in epilepsy. Lumiere went further and suggested that treatment should aim at dissolving or breaking up this abnormal state of the colloids. Lumiere's theories and experiments are deserving of more intensive investigation.

Because of its implications and clinical interest I wish to add the following clinical record to the literature:

L. B., aged eight years, first attended the Pediatric Department at Northwestern University on March 21, 1931. She complained of frequent attacks of dyspnea, which had been occurring at irregular intervals since the age of six months. She also coughed frequently, and was 10 per cent under weight. L. B. was the first-born child and had been breast fed. As an infant she was very fat. At one month of age the patient developed eczema which persisted until she was two years old, and has never recurred. The periods of asthmatic dyspnea appear every few days and at times are so severe that she becomes cyanotic.

She had measles, whooping cough, hay fever, and later pneumonia complicated by empyema (aged six years). Tonsillectomy and adénoidectŏmy were performed at four years of age. The family history was not very illuminating. The mother had died of pneumonia and heart trouble at twenty-eight years of age. The father is living and well. No history of familial asthma, hay fever, hives, or epilepsy could be elicited from an aunt who accompanied the child.

On Jan. 28, 1930, the patient had an attack of epileptic convulsions. The attack was preceded by a severe paroxysm of asthma and followed by cyanosis and coma. Since then the patient has been troubled by epileptic convulsions, which occur every week, sometimes several times weekly. It was found that the number of attacks was reduced by the asthmatic treatment. When the latter was omitted for a period of four months, the epileptic seizures increased in frequency.

On physical examination the patient was found to be of asthenic habitus and very much undernourished. Her cheeks were flushed. The respirations were frequent and labored.

Examination of the head and neck showed no noteworthy defects. The eyes reacted to light and accommodation. The ears were normal, as was the hearing. The teeth were apparently normal. The tonsils had been removed. The tongue in its anterior half presented enlarged, congested papillae which gave it a "raspberry" appearance.

The thorax was barrel-shaped and the sternum was unusually prominent. There was very little motion of the chest on respiration. The lungs were hyperresonant and emphysematous. The breath sounds were distant. Numerous fine and coarse piping râles were heard on expiration.

The heart borders were indistinct because of the emphysema. The apex was in the fifth interspace and in the mid-clavicular line. The heart tones were muffled. There were no murmurs.

The abdomen was retracted. No localized rigidity or tenderness was elicited, nor were there any palpable masses. Neither the liver nor the spleen was palpable.

The skin over the left forearm on the extensor surface persented a dry, erythematous area which had been present for months and looked like an eczematous lesion.

The extremities were normal. There were no other noteworthy findings in the routine physical examination.

Blood: Hemoglobin 75 per cent; R. B. C. 5,180,000; W. B. C. 21,450. Differential Count: Polymorphonuclears 63 per cent; lymphocytes 31 per cent; eosinophiles 5 per cent.

Urine: Straw color, sp. gr. 1,024; cloudy, reaction alkaline; few white blood corpuscles, amorphous phosphates, trace of albumin; no sugar or diacetic acid.

X-ray Examination: The frontal sinuses were not developed. The ethmoids were not aerated. The maxillary antra were small and not well aerated. The right maxillary antrum was denser than the left. The sphenoid sinuses were not yet aerated. The sella turcica was normal.

The chest roentgenogram revealed a normal cardiac and aortic outline. The cardiophrenic angle was especially prominent on the right side because of the low diaphragm.

Skin Tests: These tests were done in the Allergy Clinic and showed that the child was sensitive to chicken feathers, duck feathers, horse dander, house dust, eggs, radish, rhubarb, spinach, tomato, mustard, herring, ragweed (++++) and cockleburr.

Sputum Examination: There were no tubercle bacilli. There were numerous gram-positive diplococci, bacilli, and short chain streptococci. Eosinophiles were present, but no Curschmann's spirals or crystals.

Clinical Diagnosis: Asthma and epilepsy.

COMMENT

This eight-year-old girl is of a markedly allergic constitution (eczema, hay fever, asthma, skin tests) and, in addition, suffers from frequent epileptic seizures, which seem to be related in their incidence to the attacks of asthma. It is possible that these convulsive disturbances may be due to an alkalosis brought about by asphyxia during the asthmatic paroxysm. However, it is quite possible, that both the asthmatic and the epileptic symptoms may be due to the underlying allergic reaction.

The treatment has included calcium, ephedrin, belladonna, and attempts at desensitization against offending allergens. At times symptomatic relief is afforded but, in general, the results of treatment thus far have not been very encouraging. Lately the use of sodium thiosulphate has been resorted to, with the purpose of altering the colloid state. This treatment was suggested by Lumiere and is based on

his experimental studies. For the past three months there have been no epileptic seizures and two mild attacks of asthma. However, it is too soon to make any critical comments on the thiosulphate therapy.

SUMMARY

1. Attention is called to the very significant relation of the state of allergy to certain types of "idiopathic epilepsy."

2. A case report is presented of an allergic eight-year-old girl who has epileptic seizures in association with her asthma.

3836 W. ADAMS STREET.

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THE USE OF WHOLE CITRATED BLOOD INTRAMUSCULARLY IN A MEASLES EPIDEMIC

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IN January and February of 1932 there occurred in Providence, R. I., a widespread epidemic of measles. The epidemic was a mild form of the disease, and did not tend to cause complications. The available supply of convalescent serum was soon exhausted and the paucity of adult cases during the epidemic prevented a replacement of the supply. Physicians were therefore unable to obtain serum for use on the younger children exposed to this disease, and in a number of cities and towns were forced to use blood acquired from the convalescent cases in the homes, or in a few instances from parents who had the disease either in childhood or in youth.

The total number of cases in January and February, 1932, reported to the Providence Board of Health was 4,827, with only 10 deaths during these months. I wish to report 89 cases which were given whole citrated blood direct from the donor to the recipient in the homes. The method of administration was to draw 3 c.c. of sterile 2 per cent sodium citrate solution into a 30 c.c. syringe and withdraw from one of the veins in the donor's arm anywhere from 5 to 25 c.c. of whole blood. This was injected intramuscularly into the external aspect of the left thigh of the recipient about midway between the great trochanter and the external condyle of the femur.

The average time of injection was four days after the rash occurred in the patient to whom the child was exposed. The average amount injected was 20 c.c. The majority of the donors were brothers or sisters recovering from measles, and the blood was not taken unless the donor's temperature had been below 100° F. for forty-eight hours and no complications were present. In 14 cases 25 to 30 c.c. of the parent's blood who had had measles from ten to thirty-five years previously was used. The age of the recipients varied from four months to eleven years. After the blood was given the parents were instructed not to carry out any precautions as to isolation except in four instances where the blood was given to infants under one year old.

I have separated these 89 cases into 4 different groups because they consist of the observations of 4 different pediatricians. All of the recipients in Groups 1 and 2 were exposed to other members of their own families, only one patient being exposed to a schoolmate and in this case the recipient showed definite signs of measles. In this way

it is possible to evaluate the severity of the cases treated with whole blood as compared with the untreated cases in these families. I realize that this evaluation of necessity must be a matter of personal judgment and may be open to criticism.

The first group of 29 cases are from my own practice and were under my personal observation. I have classified the average case not treated with whole blood during this epidemic in the following way: temperature 102°-104° F., conjunctivitis 3-plus, rash 3-plus, cough 3-plus, and duration four days. The cases which were treated with whole citrated blood are shown in Table I.

TABLE I

NAME	HIGHEST TEMP.	CONJUNCTIVITIS	RASH	COUGH	DURATION IN DAYS	COMPLICATION
A. H.	101	0	+	0	2	0
D. W.	103	0	++	+	2	0
S. L.	101	+	+	0	1	0
D. D.	103	+	+	+	2	0
R. K.	101	0	+	0	1	0
C. K.	102	+	++	+	2	0
L.	100	0	+	0	1	0
A. C.	100	0	+	0	2	0
E. C.	100	0	+	0	2	0
J. C.	105	++	+++	++	3	0
B. C.	100	0	++	0	2	0
D. G.	High	0	++	0	1	0
N. O 'N.	105	+	++	+	1	0
N. F.	100	0	+	0	1	0
B. G.	101	+	+++	0	1	0
D. G.	High	+++	+++	+++	4	0
P. D.	101	0	++	+	2	0
C. O.	99.6	0	+	0	1	0
T. H.	101	0	+++	0	2	0
A. C.	98.6	+	++	0	1	0
R. C.	?	0	++	+	1	0
E. K.	99.6	0	++	0	1	0
R. K.	99.6	0	++	0	1	0
R. V.	99.6	0	++	0	1	0
V. S.	99.6	0	++	0	1	0
J. W.	101.6	0	+	+	2	0
W. K.	102	+	++	++	2	0
C. K.	102	+	++	++	2	0
C. M.	102	0	+	+	2	0

The second group, 38 in number, are tabulated from the records of my associates and from the observation of the parents, asking them to compare the donor and the recipient as to comparative severity of the measles. In every instance the donor was older than the recipient and would be expected to have a milder case than the recipient. The terms used in this group are as follows: "Mild" means slight conjunctivitis, slight cough, temperature not over 102° F. and a generalized rash. "Severe" means a typical case of photophobia and conjunctivitis, irritative constant cough, temperature 102° to 104° F., generalized confluent rash. There were 24 mild cases and 6 severe cases.

Of the latter 3 patients had received but 5 c.c. to 10 c.c. of whole citrated blood. Eight cases did not contract measles at all but were exposed thoroughly and no precautionary isolation was attempted.

The third group consists of 17 cases in an orphanage. One of my associates took 8 ounces of citrated blood from one donor, a girl who had had measles within eight weeks and gave about 10 c.c. to 15 c.c. to each of the children. These children had been exposed twice in a nursery. The first exposure and the second exposure were about eighteen days apart. None of these children had had measles. They varied in age from eighteen months to four years. Ten developed very light cases while 7 did not have measles at all.

In a fourth group I wish to give in more detail a summary of the manifestations of measles which occurred in 5 cases, because in this way some of the points which I wish to emphasize in the use of whole citrated blood as a therapeutic measure of great value in lessening the severity and preventing the complications of measles can be pointed out.

CASE 1.—Earl M., a twin, eleven years old, developed measles rash Dec. 25, 1931. Temperature 101° to 102° F., marked photophobia and conjunctivitis, severe confluent rash all over his body, marked cough, but no chest signs. He recovered in four days but coughed for one week. On Dec. 29, when his temperature was 98°, 20 c.c. of whole blood was taken from him and injected into the left thigh of Florence M., a twin sister. On Jan. 5, 1932, Florence started with a slight cough and temperature 101° to 102°. On Jan. 6 she had a generalized severe confluent measles rash all over her body which appeared within twelve hours. Temperature 101° F. On Jan. 7 there was a sudden drop in temperature to 99° during the night and the cough disappeared in forty-eight hours.

This case indicates, I think, that even in older children, whole blood may influence measles to a marked degree.

CASE 2.—Barbara W., three and a half years old, was exposed to Marshall W. on Jan. 7, 1932. Marshall W., had a temperature of 101° to 105° F., with severe conjunctivitis, moderate cough, marked rash, and no signs in the lungs. On Jan. 10 when his temperature was 98.8°, 20 c.c. of whole blood was taken and injected into the left thigh of Barbara W. On Jan. 16, ten days after the brother's rash and six days after the injection of the blood, Barbara W. began limping and complaining bitterly of pain in the left leg. On physical examination she was very tender over the outer aspect of the left thigh, and passive or active movement of the leg was impossible. The temperature was 101° F. There was no bone thickening. On Jan. 19, she was less tender, and on Jan. 20, a faint typical measles rash came out all over the body. The temperature came down to normal and the leg was much better as soon as the rash came out. There was no conjunctivitis, photophobia, or cough.

This case was interesting in that the symptoms referable to the leg were severe and were undoubtedly a reaction to the donor's blood localized to the region of injection and were very likely due to the onset of the disease itself which the serum of the whole blood succeeded in aborting.

CASE 3.—Chester W., aged five years, the brother of Thomas W., had a typical measles rash with bad cough and conjunctivitis on Jan. 21, 1932. An attempt was made to take blood from him on Jan. 25. This was unsuccessful and so 25 c.c. of

whole blood was taken from the mother, who had had measles about twenty years previously. This blood was injected in the left thigh of Thomas W. On Jan. 31, ten days after his brother's rash and six days after the injection of the whole blood, he had severe pain in his left leg and was unable to move it. A typical measles rash broke out on Feb. 1 with temperature of 101° to 103° F. On appearance of the rash the pain in the leg disappeared. There was no conjunctivitis, very slight cough, and within twenty-four hours the rash faded and the temperature dropped to 100°.

This case illustrates the use of whole citrated blood from the parent with a similar local reaction to that which occurred in Case 2, where recent convalescent blood was used.

CASE 4.—Sally L., five years old, was exposed in school to the child who sat next to her on Jan. 16, 1932. The schoolmate had a moderately severe case of measles with temperature 102° to 104°; she was sick four days, threatened with otitis media and had a cough persisting for one week. On Jan. 23, seven days after exposure, Sally L. was given 25 c.c. of paternal blood in the left thigh. The father had had measles twenty-eight years previously. On Jan. 30, Sally L. had a temperature of 101°. On Jan. 31, she had a faint generalized measles rash and a temperature of 100°; the next day the patient was well.

In this particular case the measles was influenced to a very marked degree. The father is a pediatrician and whether the potency of his blood was due to constant exposure to the virus of measles is an interesting question.

CASE 5.—R. E. G., Jr., aged two and a half years. On Jan. 30, 1931, R. E. G.'s sister had a typical measles which ran a mild course. Two days later 20 c.c. of whole blood taken from the father, who had had measles twenty-two years ago when twenty years of age, was injected in the thigh. No attempt was made to isolate this child and he ran in and out of his sister's room, sometimes actually crawling over her bed. Ten days after administration of the whole blood he developed a temperature of 104° F.: "Vomited, had pain in the left leg, was unable to move it. The next morning he was perfectly well, except that he had a blotchy rash all over the left leg." Two weeks after the first case an older brother and sister who had not had any blood injected, developed severe measles which lasted for eight days, with a temperature of 101° to 104° F. The brother, thirteen years of age, had a definite otitis media in one ear which was incised and drained for one week. No attempt at isolation was made from these two cases and R. E. G. was exposed constantly to his brother and sister. He never developed any other symptoms of measles than those mentioned after the first exposure.

This case speaks for itself. It is difficult to believe that there are any two-year-old children who are inherently immune to measles and this would be the only explanation possible unless the father's blood had conferred upon him a partial immunity.

I therefore believe that it is very worth while to use whole citrated blood in the manner which I have described in this article to protect children from three months to six years of age from the complications which are very liable to follow measles. I do not believe in giving whole blood until three to four days after the rash appears in the case to which the child has been exposed, because if done earlier than this it may prevent any signs of measles, and the immunity thus conferred will last only a short time. There is also a psychologic ad-

vantage of using blood obtained from the patient's own family instead of the serum supplied by the health department, coming as the serum does from unknown donors. It is probable that the attenuated measles which occurs may protect these children for life, or at least carry them through the years in which they might develop complications of a more or less serious nature.

I wish to express my appreciation to Dr. Henry E. Utter, Dr. William P. Buffum, and Dr. Reuben C. Bates for allowing me to use their cases in this article.

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ANTIQUES OF PEDIATRIC INTEREST

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THE ceremony of touching for scrofula, the King's Evil, was performed in England from the time of Edward I until the end of Queen Anne's reign (with the exception of during the reign of William and Mary), a period of nearly 700 years.

In the reign of Henry VII, the presentation of a piece of gold was first generally introduced. This was the angel-noble, a circulating gold coin of the time, on which an angel is represented standing with both feet on a dragon. A warrant issued in the reign of James I for the special coining of angels as touch pieces shows that although they were current coin, they were also made ready pierced for the purpose of suspension about the sufferer's neck during the ceremony of touch-

Gold touch piece, Charles II, circa 1662 (diameter 7/8ths inch).

ing. From the days of Charles II to those of Queen Anne, this gold coin being no longer current, a special gold medalet of the type illustrated, varying only in size and the name of the reigning sovereign, was struck and perforated for the ceremony.

The immense popularity of the ceremony is shown by the entry in *Evelyn's Diary* for March 28, 1684: "There was so great a concourse of people with their children to be touch'd for the evil, that six or seven were crush'd to death by pressing at the chirurgeon's doore for tickets."

The following is Evelyn's description of the ceremony:

"6 July, 1660. His majestie began first to touch for ye evil, according to custom thus: his majestie sitting under his state in ye banquetting house, the chirurgeons cause the sick to be brought or led up

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to the throne, where they kneeling, ye king strokes their faces or cheekes with both his hands at once, at which instant a chaplaine in his formalities says, 'He put his hands upon them and he healed them.' This is said to every one in particular. When they have ben all touch'd they come up againe in the same order, and the other chaplaine kneeling, and having angel gold strung on white ribbon on his arme, delivers them one by one to his majestie, who puts them about the necks of the touch'd as they passe, whilst the first chaplaine repeats, 'This is ye true light who came into ye world.' "

The register of those touched for the King's Evil by Charles II extends from May, 1662, to April, 1682, and gives the number of persons touched by the king for the evil as 92,107, as many as 600 being touched at one ceremony.

Belief in the efficacy of the royal touch for the cure of scrofula was not confined to the ignorant. Richard Wiseman, in *Severall Chirurgicall Treatises,* 1676, writes:

"But it is not my business to enter into divinity-controversies; all that I pretend to, is first, the attestation of the miracles; and secondly, a direction for such as have not opportunity of receiving the benefit of that stupendous power."

And the following is his answer to those who questioned the miraculous cure:

"For since it cannot be denied that many go away cured, some will impute it onely to the journey they take, and the change of air; others to the effects of imagination; and others to the wearing of gold.

"The first of these is easily confuted by the hundreds of instances that are to be given of inhabitants of this city, who certainly could meet with little change of air, or indeed of exercise, in a journey to White-hall. The second is readily taken off by the examples of infants, who have been frequently healed, though they have not been old enough to imagine any thing of the majesty, or other secret rays of divinity, that do attend kings, or do any other act that way to contribute to the cure. The third hath more of colour in it because many that have been touched, have upon loss of their gold felt returns of their malady, which upon recovery of that have vanished. But in this case also we have many evidences of the contrary.

"For his Majesty's royall father in his great extremity of Poverty had not gold to bestow, but instead of it gave silver, and sometimes nothing; yet in all those cases did cure; and those that were cured by his blood wore no gold.

"Now whereas upon the loss of the gold some have found damage; I would know, whether any of them were relieved by the wearing any other gold *then* what the king gave them."

Critical Review

ALLERGY AS RELATED TO OTOLARYNGOLOGY AND PEDIATRICS

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IN A PREVIOUS review in this Journal, Smyth[1] made a comprehensive survey of the most important articles appearing in the literature on the subject of allergy in general. In another review, Dean[2] gave an interesting account of the recent advances in pediatric otolaryngology. In the present review, it is intended to make an analysis of those publications having a relationship to both the otolaryngologist and the pediatrist. The commonest manifestations of allergy are those which occur in the nose and paranasal sinuses, and while this area may be the only site involved, allergy is frequently manifest in other parts of the body and in other ways. It is often necessary for the otolaryngologist to determine whether some condition such as headache, gastrointestinal disease, bronchitis, asthma, eczema or recurrent colds, as diagnosed by the pediatrist, is associated with a nasal allergy. The presence of a definite nasal allergy should suggest the allergic origin of the various conditions mentioned.

The responsibility of diagnosis and treatment of certain infections of the upper respiratory tract in children, such as acute and chronic rhinitis, sinusitis, tracheitis, bronchitis and laryngitis, should rest on both the otolaryngologist and the pediatrist. Although these disturbances may be due to infection, they are frequently manifestations of allergy, and if proper treatment is to be instituted, the infections must be differentiated from those conditions of an allergic nature. It must also be emphasized that an infectious process may occur in a child known to be allergic, so that attention should be directed to this factor as well as to the infection. The points relating particularly to coexisting allergy and infections in adults have been emphasized in former communications.[3, 4, 5, 6, 7] In the Pediatric Allergy Clinic of the Washington University Dispensary, we have had opportunity to observe a large number of children with seasonal and nonseasonal nasal allergy with and without associated bronchial asthma. Cases of eczema and selected cases of gastrointestinal disease, headache, frequent head colds, paranasal sinusitis, recurring acute bronchitis, chronic bronchitis, bronchiectasis and various forms of dyspnea, have been observed with the idea of determining whether or not allergy was a factor in the production of these conditions. In many of these cases the diagnosis of an associated nasal allergy suggested the allergic origin of the other condition. It was found that it is especially important in dealing with the respiratory conditions to determine whether we were dealing with a pure allergy, an infection or an allergy with superimposed infection. A proper diagnosis of these various conditions and their relation to allergy can be established only after taking a detailed clinical history and making certain physical and laboratory examinations.

Reference to the relationship of allergy to infection may be found only in the most recent literature on the subject of frequent colds, sinusitis, and bronchitis. The relationship of sinusitis and acute nasal infections to asthma and other forms of allergy has been greatly clarified by a careful study of the differential diagnosis between allergy and infection, and has been emphasized by Dean,[8, 9] Carmack,[10] Richards,[11] Brown,[12] Cassady[13] and McLaurin.[14]

Cohen and Rudolph[15] in a recent report emphasized the importance of differential diagnosis between allergic and infectious conditions of the upper respiratory tract in children.

Consideration must be given to the factors which indicate the allergic basis for the complaints. These are: (1) the family history, (2) past history of allergy, (3) presenting symptoms, (4) skin tests and (5) blood examination for eosinophilia. From the otolaryngologic standpoint, the following factors are to be especially considered: (1) the nasal symptoms, (2) rhinoscopic examination, (3) nasal smears, (4) roentgenologic examination of the sinuses and (5) histologic examination of the nasal and sinus tissues.

A detailed clinical history in these cases is of the utmost importance. A study of the family history of allergic patients will reveal the fact that a much larger number of relatives are found to be affected with manifestations of allergy than is the rule in other families. The studies of Cooke and Vander Veer,[16] Spain and Cooke,[17] Adkinson[18] and Balyeat,[19] show positive family histories in 40 to 60 per cent of the asthma cases in their series. Among the normals, investigated in some of these studies, a positive family history occurred in only 7 to 9 per cent. Coca[20] and his associates have pointed out that heredity not only plays a part in the choice of the individuals affected, but also more or less determines the nature of the malady by designating the predisposed shock organ. The evidence seems to indicate that the age of onset is more or less predetermined by hereditary factors as is also the nature of the atopens or allergens to which the patient tends to become sensitive. Cooke and Spain,[21] and Cooke,[22] have reported that when there is a positive history of allergy in both parents, approximately 75 per cent of the offspring will develop manifestations of allergy before the tenth year. With a single inheritance, 31 per cent, and with no history of inheritance, 20 per cent develop manifestations before the tenth year. Of all children with bilateral inheritance, 70 per cent will eventually develop symptoms, and of those with a unilateral history about 50 per cent. The earliest manifestation of allergy which appears in infancy is eczema. This is often replaced by the respiratory symptoms later. During the first three years of life, foods are the outstanding factors and after this age, the inhalants are to be considered. Hypersensitivity to foods and infections in infants, tends to disappear between the age of five and ten years but hypersensitivity to the inhalants tends to persist. According to Rowe,[23] however, food sensitization may remain as a major factor or the sole cause of symptoms into adult life, in spite of the fact that skin tests may be negative. Asthma developing between the age of three and thirty years is usually caused by the inhalants. The onset is often gradual and is usually preceded by the nasal manifestations. Asthma appearing after the age of thirty years is usually associated with infections and is also gradual in its onset. The clinical history frequently shows that the allergic child has other manifestations of allergy, such

as eczema, urticaria, gastrointestinal symptoms, asthma or hay fever, either recently or in the past. In some cases, the manifestations of the food allergies are not acute and lead to evidences of mild disturbances such as anorexia, malnutrition, nervous irritability and sleeplessness. The examination of the blood usually shows an eosinophilia and positive skin tests are usually found. In the infectious cases due to infection without allergy, the family history is usually negative for hypersensitive individuals; rarely are there any other manifestations of allergy, the blood shows no significant eosinophilia and skin tests are negative.

Since the clinical picture of acute rhinitis and acute paranasal sinusitis is well known, only a brief consideration of this phase of the subject is necessary. Attacks of acute rhinitis usually run a typical course, lasting from five to twelve days, after which there is usually an immunity lasting several weeks or if the attack is uncomplicated, there is a complete resolution of the process. There is generally a history of physical exposure or of contagion. The attack is accompanied by fever, malaise and other well-known symptoms. The onset is not related to food or inhalant contacts. The examination of the nose shows a swollen, usually hyperemic membrane with mucopurulent secretion which shows the presence of numerous pus cells. Roentgenograms of the sinuses are not often significant. When acute rhinitis does not undergo resolution within a reasonable period of time, however, a complicating sinusitis usually manifests itself with the symptoms of persistent mucopurulent discharge, positive roentgenographic findings and general symptoms of infection. In chronic paranasal sinus infections, it is particularly important to differentiate between allergy and infection and to take into consideration that an existing chronic infection may be associated with an allergic process.

It is also important to mention that the manifestations of allergy may be noted for the first time following one of the common contagious diseases of childhood. Peshkin[24] found that pertussis was the most frequent causative disease. Measles and scarlet fever were also mentioned. Other infections such as pneumonia and influenza may also be responsible. What appears to be a sinus infection following these diseases should, therefore, be carefully investigated because of the fact that nasal allergy may originate in this manner.

In the consideration of allergy as it manifests itself in the nose and paranasal sinuses in children, information in the history regarding the criteria which characterize the state of hypersensitivity must be obtained, but in the analysis of the clinical history, physical and laboratory findings, one may expect great variations. Sometimes diagnosis is prompt and easy but often it can be established only after periods of observation. We usually think of the nasal symptoms as being characterized by attacks of sneezing, nasal obstruction and the discharge of serous or mucous material. Picking at and itching of the nose, rubbing of eyes and clearing the throat or a dry cough may be prominent and characteristic symptoms. There are a great many instances, however, in which all of these symptoms are not present. Although sneezing may be a prominent symptom, in children it is frequently absent. The child may show only signs of nasal obstruction and nasal discharge. Obstruction may be more or less constant or it may be intermittent. Discharge may be profuse and watery or it may

be entirely postnasal in the form of thick mucus. A child may exhibit only the symptoms of transitory attacks of nasal obstruction. Attacks of nasal allergy are usually not related to contagion but frequently appear with an inhalant or food contact. Fever or constitutional symptoms are rarely present. Typical attacks are usually recurrent every few days or every few weeks. In certain cases, however, they may appear with long periods of remission, resembling in this respect attacks of acute rhinitis. It is important to note other manifestations of allergy may exist in other parts of the body with those in the nose. Children often have gastrointestinal symptoms such as gas, belching, distention, cramps, pain or diarrhea at the same time. Local or generalized headache, angioneurotic edema, bronchitis or asthma may also occur. Attacks of nasal allergy may alternate with attacks of acute rhinitis. Following an attack of acute rhinitis or bronchitis, nasal symptoms may become more severe or they may entirely subside for several weeks. Acute infection frequently increases the degree of hypersensitivity in allergic individuals, often precipitating symptoms after a period of apparent quiescence. The patient, therefore, may react to a slight exposure which in the absence of infection would not be sufficient to cause symptoms. Nasal symptoms may subside during the existence of some other manifestation of allergy such as urticaria. Nasal symptoms may be present or absent with allergic headache. During attacks of nasal allergy we must bear in mind that reactions are also occurring in the paranasal sinuses. The swelling of the lining membranes, the increase flow and consequent retention of secretions may produce local pain or headache.

On examination of the nose in allergy, characteristic changes in the mucous membrane are found; they are characterized by a pale, swollen edematous appearance of the turbinates and an abundance of mucoid secretion. Gross polypoid changes are rarely present in young children but may be found not infrequently in older children. During the state of active symptoms, these changes are easy to recognize but during the quiescent periods, the membrane may appear quite normal or may appear pale and dry with thick mucoid secretion, and the picture may not be easy to recognize.

The most important laboratory method used in diagnosis is the microscopic examination of the nasal secretions for the presence of eosinophiles. In the collection of nasal secretion for examination, it is necessary to obtain mucous material because it contains the cells which are to be examined. Thin, watery material usually shows very few, if any, cells. In children, instead of swabbing the secretion from the nose, simply direct the child to blow the nose on some waxed paper and transfer the material to glass slides. It is advisable to make two or three smears because the eosinophiles may be found only in certain parts of the specimen. They may be entirely missed upon the examination of only one slide. The smears should be stained by Wright's stain in the same manner as blood films. The number of eosinophiles observed may not be constant because several factors which cause them to appear may vary. During the complete inactivity, they should be absent. Frequently, however, during an apparent stage of inactivity, there are mild transitory reactions which do not give rise to noticeable symptoms, yet the secretions will reveal the presence of many eosinophiles. If an acute infection occurs, they may be either present or absent. They may be found in considerable numbers along with the

pus cells or neutrophiles, or due to the relatively large number of pus cells, they may appear diminished. As the cold subsides, the pus cells disappear and the eosinophiles continue and reappear in relatively increased numbers. In some cases, however, there may be few or no eosinophiles during an acute rhinitis. In these cases, the manifestations of allergy may entirely disappear for a certain period of time following the subsidence of the acute infection. The gross examination of secretions without cytologic study has proved to be very unreliable in drawing conclusions as to the presence or absence of pus. Clear secretion may show pus cells or eosinophiles or both. Yellowish mucopurulent secretion may contain pus cells, both types of cells, or may show only large numbers of eosinophiles.

If a chronic infection of the paranasal sinuses becomes associated with an allergic process, both eosinophiles and pus cells are found in the secretions. An exacerbation of the infection may result from repeated acute infection or from allergic reactions following contact with an offending allergen. Allergic reactions may cause considerable increase in an already existing edema.

In the histologic examination of the nasal tissues in allergy, in infection, and in allergy with infection, the picture is comparable to the cytology of the nasal and sinus secretions. Edema of the tissues is an almost constant finding in allergy and is usually very marked; but it may also be present with infection. Eosinophilic infiltration of the tissue is a characteristic feature of allergy, while acute rhinitis is characterized by some edema and neutrophilic infiltration. In combined allergy and infection, both types of cells are found. Lymphocytic and plasma cell infiltration are present in both types of reactions. Chronic infection produces connective tissue proliferation in various degrees.

The roentgenographic findings in the paranasal sinuses in allergy as well as in infection, are positive in a very large percentage of cases and cannot be differentiated from each other. In allergy, positive findings may be purely transitory, being present at one time and absent at another. It is unfortunate that in many of the reports in the literature on paranasal sinus infection in children, so much reliance has been placed upon roentgenographic findings and the cytology of the secretions has been so greatly neglected.

Too much reliance should not be placed on the performance of skin tests and their interpretation in the diagnosis of allergy. A positive reaction indicates nothing more than a clue as to past, present or future possibilities. Its significance must be determined by further clinical observation. On the other hand, negative tests do not rule out the possibility of existing allergy. Kahn,[25] for example, has found that skin tests in infants and young children, suffering with pollen asthma and hay fever, are frequently entirely negative or only slightly positive. He believes that such weak positive tests actually indicate a minor degree of hypersensitiveness and he urges that advantage can be taken of this low degree of sensitiveness in initial or early stages of asthma to render these children free or nearly free from attacks by proper precautions against pollen overdosage.

In the management of acute and chronic tracheobronchial conditions in children, the otolaryngologist is frequently called upon to determine the possible relationship to certain pathologic disturbances in

the nose and throat. Cooke[22] has described a peculiar cough which he frequently found associated with allergic coryza. The cough is violent and paroxysmal in nature and is frequently accompanied by vomiting. He believes it is caused by hypersensitiveness and discusses the difficulty of differentiating this cough from pertussis. Duke[26] has also called attention to the occurrence of allergic bronchitis and states that it is often incorrectly diagnosed as tuberculosis, chronic bronchitis and bronchiectasis. A. Brown[27] asserts that a spasmodic bronchitis sometimes inaugurates an attack of asthma in children. He believes that in children this type of bronchitis occurs more frequently than true bronchial asthma. Rowe,[23] Colmes,[28] Colmes and Rackemann[29] and Kahn[30] state that a dry, irritating cough is a symptom of sensitization of the trachea and the bronchi and point out the importance of recognizing these atypical cases of asthma. The examination of the nose in these cases may show the picture of allergy or infection. Attacks of asthma may follow immediately an attack of nasal allergy. An acute infection of the nose may also precipitate an attack of allergic bronchitis or asthma. Walzer[33] states that when infection precipitates attacks they usually occur several days after the onset of the infection, while in cases of pure allergy the attacks usually are produced immediately. The presence of upper respiratory infection, therefore, such as the common cold, paranasal sinusitis and tonsillitis is often responsible for the precipitation of an allergic bronchitis or asthma. The proper treatment of these upper respiratory conditions increases the resistance of the patient and prevents the occurrence of the infections and thereby simplifies the management of the allergy.

In the treatment of these cases it is evident that the control of the allergy is of primary importance. An attempt should be made not only to eliminate the offending allergenic substances but to eliminate if possible all nonspecific factors. The nutritional state of the patient should receive due consideration. All infection, such as that existing in the paranasal sinuses, teeth, tonsils and adenoids, should be eliminated in cases in which these procedures are indicated. In the performance of surgical procedures it is particularly important to avoid the stages of active allergic symptoms; this is especially true regarding active hay fever. All cases of allergy should be under control before resorting to surgery. In children, as well as in adults, the observations of Rackemann and Tobey,[31] Bullen[32] and others have shown that in a large series of cases the removal of the tonsils and adenoids has shown no definite influence in the improvement of the existing asthma.

Walzer[33] states that the removal of the tonsils and adenoids in an allergic individual is frequently followed by the development of nasal allergy, or asthma or both. Many cases of pollen hay fever or asthma date the onset of their first symptoms from a tonsillectomy, and it is impossible to consider the coincidence of the two conditions or events as purely accidental. The question may well be raised as to whether the infection which instigates the procedure may not have been responsible rather than the operation itself. We have found that in many cases of children with allergy a tonsillectomy was definitely indicated, but with careful attention to the control of the allergy, the occurrence of untoward complications could be avoided with reasonable safety.

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MONDAY AFTERNOON SESSION
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Round Table Conference on Allergic Conditions

Leader: Dr. Bela Schick; Assistant: Dr. J. E. Gonce.

DR. SCHICK.—It is my intention to make only short introductory remarks. I would like to have a very lively discussion, which need not be limited to the problems I shall mention.

When one talks about allergy, it should be remembered there are two things to be considered: First, allergy as a very wide term, meaning all kinds of altered reactivity of the organism due to previous administrations of a foreign substance. Every disease, both the acute ones and to a greater extent all chronic diseases, may show allergic features. Second, we can include in our discussion the so-called allergic diseases such as asthma, hay fever, eczema, urticaria, etc. A better title for these diseases would be "hyperergic diseases."

(Dr. Schick abstracted his remarks as printed in the February, 1933, issue of the JOURNAL OF PEDIATRICS.)

DR. J. E. GONCE (MADISON, WISCONSIN).—In opening the discussion of Dr. Schick's summary on the general subject of allergy, I would like to emphasize the fact that the proper handling of cases of asthma, hay fever, eczema, etc., is an intricate procedure, one which requires the closest attention to every detail and familiarity with the latest theories and practices of the specialists in this field of medicine. A casual interest in allergic disorders is certainly paralleled with bad results.

A few of the practical points connected with the diagnosis and treatment of allergic disorders which impress me as being of fundamental importance are concerned with (1) the selection of materials, (2) the use of guides in pollen therapy, and (3) methods of administration of protein extracts.

(1) The materials used for sensitization tests and for desensitization must be absolutely reliable. In my experience glycero-saline extracts are more sensitive but on account of the danger of causing constitutional reactions must be preceded by scratch tests, thereby making their use too expensive for general use. Many specialists in allergic disorders use powders for scratch testing but most of these men manufacture their own in order to be certain of their allergic activity. Where it is impracticable or impossible to prepare protein extracts for one's own use, as is the case for most of us, it is necessary to exercise the greatest care in the selection of a commercial manufacturer from whom to purchase extracts. In this connection an experience of mine last winter is enlightening. In answer to questions concern-

ing the detailed preparation of pollen extracts, one well-known firm replied, "In the beginning the writer would say that our house is probably not in any way different from any other commercial house and while we have no objection to offering the general routine of our methods of manufacture, nevertheless, there are many items connected with the manufacturing of proteins and pollens that are considered manufacturer's secrets." Another house hedged on some of the questions and the third firm addressed completely answered all questions and denoted their willingness and even desire to supply all information within their power to furnish. Now that Stull and Cooke and their coworkers seem to have definitely shown that the allergically active factor of pollens resides in the albumin fraction and have suggested the standardization of pollen extracts on a protein nitrogen basis, it is quite likely their recommendations will be accepted and the preparation of various extracts for testing and therapeutic purposes become a uniform and reliable procedure practiced by all commercial houses alike.

In regard to the stability of extracts prepared for therapeutic purposes, I believe everyone at the present time agrees that the glycero-saline extracts are the most stable. In a recent issue of the *Journal of Allergy*, it is stated that 31 out of 73 specialists use extracting fluids containing glycerine.

(2) The use of various guides in pollen therapy is now a well-established procedure and may be considered under three divisions. First, determination of the patient's skin sensitivity to serial dilutions of the offending pollen will prevent waste of time by an unnecessary number of weak doses and will also help to avoid the administration of initial doses large enough to cause constitutional reactions.

Second, application of skin tests in serial dilutions during the course of treatment is of decided value in estimating the frequency and number of doses necessary to bring about satisfactory desensitization in the individual case. Although it is not universally agreed that pollen therapy influences the severity of the response of skin tests, the opinion of many men, especially Dr. Duke of Kansas City and Dr. S. T. Brown of Washington, who use large doses, is that there is not only a relationship between pollen therapy and skin sensitivity but a diminution in skin tests may be indicative of a lessened clinical sensitivity as well. In proof of this belief, it has been shown that failure to obtain clinical improvement in a hay fever patient whose skin test has been changed by therapy from a strongly positive to a weakly positive or negative reaction, may be due to extra-pollen sensitivity.

Third, the extent of the local reaction from each subcutaneous injection of pollen extract is of considerable help in estimating the dose of the following injections. In using this guide, it is necessary to place the injection superficially in the subcutaneous tissues because the deeper method of injection is less apt to produce a local reaction.

(3) As to the method of administration of protein extracts, I would like to encourage the use of the Duke method. Although there are certain specialists in allergic disorders who like to poke fun at the use of the tourniquet and adrenalin-ephedrin mixture, I feel quite certain this method makes the administration of protein extracts almost "fool-proof." It has several advantages in that it permits rapid increase in the amount of protein extracts given, the administration of doses of a size far beyond those of the unmodified injection method, and, in the case of perennial treatment, permits the lengthening of the interval between injections to two, three or four weeks without danger of constitutional reaction. Dr. Duke himself says this interval may be stretched to two or three months.

I personally have dropped the use of the tourniquet because soon after adopting the Duke method of injection I noticed on the third, fourth or subsequent application of the tourniquet, the child's arm immediately became terribly discolored. Consequently, I leave off the tourniquet and minimize the possibility of injecting directly

into a blood vessel by first drawing back the plunger of the syringe before making the injection. The mixture of one-third adrenalin and two-thirds ephedrin (3 per cent solution) in amounts of 0.2 c.c. combined with the extract causes an almost immediate blanching of the skin where the injection is superficially placed and the rate of absorption, I am sure, is retarded just about as much as when the tourniquet is used.

I have only a couple more things to say. I happened to think when Dr. Schick was speaking of status asthmaticus, that our adult medical service has had occasion to treat several patients with this condition by means of bronchoscopic cleansing of the trachea and bronchi. One patient is a traffic officer in Madison who obtains immediate relief by this treatment. He then remains free from symptoms for many months.

In closing I would like to ask Dr. Schick to state his opinion of the relative merits of the ideas on tuberculosis of Heimbeck of Oslo and Myers and Stewart of Minneapolis.

DR. SCHICK.—About the influence of repeated injections on the intensity of the skin reaction, it can be stated that a large dose may have an attenuating effect upon a following skin test. Similar observations are made in tuberculin treatment. Frequently a Pirquet test made twenty-four hours after a large dose of tuberculin (1 mg.) will be smaller or even negative. The Pirquet test will become positive again after an interval.

Asthmatic patients free from attacks for several years still may have about the same intensity of the skin reaction as at the time of attacks. Apparently the reactivity of the skin is dissociated, so to speak, from the asthmatic reaction of the respiratory tract. This may be due to treatment or to aging (maturing). An eczematous patient may lose his eczema and exchange the eczema for an asthma. Apparently the skin changes its reactivity and the respiratory tract starts to react in an abnormal way. In eczema and asthma, we frequently find that when the eczema improves the asthma gets worse or, as the asthma gets better, the eczema appears. There is an interrelation between the two organs, the skin and respiratory tract. There can exist a complete dissociation, so the eczema can disappear while the asthma remains. It is possible to obtain a very strong skin reaction to a certain protein although the asthma is not due to this protein or, you can encounter just the reverse; a relatively weak reaction (± reaction) to a protein which is responsible for the asthmatic attack.

As to the use of adrenalin and the tourniquet, these procedures are helpful; both slow down the absorption. Adrenalin brings about a vasoconstriction; the tourniquet compresses the lymph channels. In all cases where we suspect the patient is very sensitive to the substance to be injected, i.e., horse serum, such procedures should be taken into consideration, especially the use of the tourniquet. The same can be accomplished in an easier way by injecting higher dilutions of the substance.

The story of a policeman who was treated during his attacks by sucking out the plugs with the bronchoscope is very interesting. Of course, bronchoscopy is a little more dangerous in children than in adults.

Concerning the idea of Heimbeck in Oslo, as to whether it is better to be infected with tuberculosis and become reexposed or to be infected with tuberculosis with no previous tuberculous infection, I read very carefully the article by Dr. Stewart in which he expresses the latter theory. The prevailing theory is that the first infection with tuberculosis in a mild form immunizes to a certain extent against a reinfection later in life. The immunity of the adult against tuberculosis is based upon the effect of the preceding infection in childhood. In an institution for the treatment of tuberculosis in Oslo, Heimbeck divided the nurses into two groups, in the one were the tuberculin positive and the other, the tuberculin negative nurses.

He studied these two groups of nurses during their stay, as they were exposed to tuberculosis and found the nurses who had a positive tuberculin test on admission were better off in that not such a large number of them developed an active tuberculosis. Many more of the nurses who came in with a negative reaction indicating they had no previous infection with tuberculosis, developed active tuberculosis. He used this observation as a reason to introduce active immunization with B. C. G. against tuberculosis among nurses and he was very much satisfied with it.

Dr. Stewart found in his examination of 10,000 school children that several children who did not show any form of tuberculosis for several years before, on exposure developed a very mild tuberculous infection. On the other hand, children who were positive before to tuberculin and had some calcified foci in their lungs, developed a very active tuberculosis.

I still believe that much depends on the quantity of tubercle bacilli entering during exposure. If an individual has been exposed to a very large amount of infection, this person is in danger whether he had a previous infection with tuberculosis or not. We are afraid of massive reinfections, as the immunity against tuberculosis conferred by a previous infection is only a limited one. It is sufficiently strong for a mild reinfection but it does not help against a very violent one. I think it is too early to accept Stewart's viewpoint as final. We may still adhere to the idea that a small first infection produces a certain amount of immunity against a new invasion.

(Discussion by Dr. Bell not sent in for publication.)

DR. BLATT (CHICAGO).—Dr. Schick, you expressed a thought I believe should be stressed a little more, namely, the relationship between allergic phenomena and infectious diseases. In 1911, when I worked in your dispensary in Vienna, you emphasized the fact that some of the kidney complications of scarlet fever were allergic. At that time, you expressed the thought that in all probability the glomerular nephritis coming on in the third week of scarlet fever was a secondary phenomenon not due to a local streptococcic infection but probably to an allergic phenomenon of streptococcic origin. I have always felt that expression was worth passing on and nothing in the interim has changed my belief in this statement.

I think the term "allergy" is not satisfactory, as it is applied now. It has seemed to me that all forms of dermatitis should not be classified as allergic even though they express somewhat similar phenomena. For instance, a dermatitis due to sun rays, a dermatitis due to an irritant, a dermatitis due to feathers, a dermatitis due to some other immediate contact agent, should not be classified with those allergic phenomena associated with changes in protein sequential to liver dysfunction or direct gastrointestinal absorption without liver detoxication. It is quite apparent that the same principles which underlie Besredka's attempt at immunization through systemic means is influencing us in our allergic immunization. As you stated, it is quite possible to apparently arrest the asthma and have the skin retain its tendency toward urticarial phenomena on an allergic basis. I think many of these so-called allergic phenomena are much more closely related to dermatitis and are inflammatory rather than primarily exudative.

Based upon findings of the United States Department of Agriculture, the milk shed of Chicago is definitely known and the open pasture has definite dates. In the spring when the cattle first are turned out to pasture, large numbers of weeds are ingested and many of these contain active glucosides which may be the source of some of our allergic skin phenomena such as lichen urticatus.

As to infection with tuberculosis, Dr. Jaffe has expressed himself as being in accord with Stewart's opinion and I am accepting this theory. The large amount of pathologic material at Cook County Children's Hospital seems to show many serious effects of superimposition of tuberculous infection rather than primary

sensitization and primary complex dissemination. Last winter I saw a number of postmortem examinations on generalized tuberculosis with a primary complexion that was apparently entirely healed and I am of the opinion the primary vaccination with tuberculosis was not effective in protecting these cases. From time to time, I have seen a general dissemination from a primary complex but these cases are comparatively rare.

I would like to ask a question in regard to the use of dextrose, which reports from Guy's Hospital seem to favor. It is thought its effectiveness has to do with liver protection; possibly that it has to do with increasing of the detoxified reaction in the liver rather than any relationship to the blood sugar content primarily. I tried this procedure in two or three cases, in one of which I had very unusual success. Not only did the patient, an adolescent girl, who had asthma all her life, react favorably so far as the asthma was concerned, but she gained a large amount of weight.

DR. SCHICK.—The first question was about allergy in infectious diseases, especially in scarlet fever. Dr. Blatt quoted me correctly. I believe that fourteen days or three weeks after the onset of scarlet fever, a period of increased sensitiveness starts and all postscarlatinal diseases are the expression of this allergy (immediate) to a germ having survived from the time of the original scarlet fever process. Some authors feel that the first part of the scarlet fever process is also allergic in nature. I think my original idea is more correct, that the first symptoms in scarlet fever are due primarily to a toxic substance and only the postscarlatinal diseases are allergic in nature. It is interesting that similar observations have been made in typhoid fever and measles. In order to be careful as to how far one should go with theories, I have left open the answer to the question whether the nephritis and the other postscarlatinal conditions are the effect of the streptococcus and its toxin.

Dr. Blatt pointed out that it is very hard to apply the term "allergy" to so many different types of symptoms and I agree. However, allergy is a necessary term; we need such a word for the "altered reactivity." If we make clear that what is especially important from the practical viewpoint is the hyperergic or anaphylactic reaction, there will not be much room for misunderstanding. Severe anaphylaxis, characterized by a shock endangering life, does not occur so frequently. If one considers how many millions of injections of serum are given and how few cases of real anaphylactic shock are observed, one will realize that it is fortunately very rare. Anyone who has seen such an anaphylactic shock will never forget it and will be very cautious thereafter, in injecting serum, particularly intravenously.

The good effect of the injection of glucose is difficult to explain. It may be helpful in stimulating the function of the heart. Another factor may be the improvement of the liver function as during the anaphylactic shock, the glycogen of the liver disappears. The circulation also will be benefited by the supply of fluid.

DR. LEWIS WEBB HILL (BOSTON).—There is a large group of skin conditions in infancy we call infantile eczema and I am quite sure we are in reality dealing with a number of different, probably unrelated, diseases. We must split apart this group as far as we can, by close observation of the skin and very careful study as to etiology, for we never will get anywhere with infantile eczema until we do.

If one considers the history of dermatology in the last fifty or seventy-five years, one sees that is what is happening. The dermatologist of olden times was confronted by an individual with a red skin eruption and he gradually noticed these skin eruptions were different. Scabies used to be called eczema, so did psoriasis and pityriasis rosea. We must go through the same process with our infantile

eczemas before we can really understand them. I believe 60 to 70 per cent of the cases of infantile eczema are of allergic origin but there are, as Dr. Bell has said, a good many causative factors other than allergy. I think we must take fungus infestation into consideration. In adult dermatology at the present time, there is a tremendous interest in fungus infestation of the skin with the epidermophyton group and the *Monilia albicans* or thrush group.

I am very much interested in this as regards infants and children and am trying to determine by intracutaneous skin tests with various fungi, what cases can be put into the fungus group. The difficulty is that oftentimes food allergy and fungus infestation occur together and I am quite sure it is the allergic child who is especially susceptible to fungus infestation. This work is not far enough along at present to say definitely that we can, by means of skin tests or by any other method, determine exactly which cases are due to fungus infestation and which are not, because culturing the fungi from the skin means very little. Making scrapings of the skin and finding them under the microscope means little as they also occur on so many normal skins. Both of these methods are somewhat complicated for average use.

Skin tests with various fungi show a fair number of positive reactions and I have brought a few pictures of what would seem to be fairly typical fungus eruptions. These pictures all represent probable monilia infection; that is, thrush of the skin. I have had positive tests in cases one would certainly call ordinary "eczema." Fungus infestation, however, is probably of relatively small importance in infantile eczema and we must go back to allergy to account for most of the cases.

We should do skin tests on most cases of infantile eczema as we get a good deal of information. This is perhaps more theoretical than practical because a great many times we find by the skin tests nothing whatever to help us in the actual treatment of the child. A five-month-old baby who has never eaten an egg may give a strong test to egg white. That does not help much in the practical treatment of that baby, but it does tell us that the baby is allergic and I consider the reaction to egg white in young infants a stamp of allergy. It identifies that baby as being of an allergic constitution and as Dr. Schick said, sensitization through the placenta is probably very common and I am quite convinced a great many cases of infantile eczema start by sensitization to egg white through the placenta.

Egg white is the most difficult of digestion of any protein and if one eats a raw egg, some of the egg white goes unchanged through the intestinal mucosa into the general circulation. Some time ago I got some serum from an egg sensitive child with eczema and injected a little into my forearm. The next day I ate some cookies and within fifteen to twenty minutes, a big wheal developed on my arm.

I made some passive transfer tests for a baby with very bad eczema, whose skin was so bad I could not do ordinary skin tests. I put into the arm of the baby's father about 30 injections of the baby's serum in very small amounts and unknown to me, this man was in the habit of eating a raw egg every morning for breakfast. He ate a raw egg the next morning and his arm was enormously swollen for two or three days and the reaction persisted for several weeks. The serum of an eczematous child sensitive to egg may be a powerful thing and if passive transfer tests are done, we must be careful to use only very small amounts of serum or to dilute the serum considerably before injection.

I use a type of skin scratcher that I devised. It is not so easy to do skin tests with a needle or a knife on a baby, as the baby struggles, he has to be held down with one hand, and it is very difficult to make the scratches exactly the same depth and length and it is important to do so in order to read the tests accurately. This instrument is simply a small punch, like a leather punch; it is sharp on the end and makes a circular scratch.

I have derived a great deal of pleasure and profit from reading Dr. Moro's book on Eczema. It is a masterly exposition of the subject but, as Dr. Schick said, it is very interesting to see how little attention the Germans have paid to allergy and skin testing. Dr. Moro in the preface of his book says he did not attach much importance to skin testing until he had written about half the book; he then decided to try them and see whether they were worth while and he became most enthusiastic about the allergic theory of eczema.

He believes sensitization to egg in utero is the primary step in the development of a great many infantile eczemas. The child being stamped as an allergic individual, the allergy may branch out in a number of different directions and he may become sensitized to a great many other things as well and have a multiple sensitization. Why some infants become sensitized and some do not is obscure; it may depend upon hereditary factors, or possibly on quantitative differences in the allergen ingested. This is a very attractive theory and fits in well with the facts of eczema as we observe them.

Another interesting thing about egg white, Woringer, who writes so well on allergy, believes there are two kinds of egg sensitive babies, one in whom there is simply skin sensitivity and no antibodies in the blood; the other in whom there is skin sensitivity plus antibodies in the blood. He believes an eczematous child cannot be cured by removing egg from the diet even if he is sensitized to egg, and I am rather inclined to agree. I have seen innumerable older children sensitive to egg with positive skin tests, but I have never seen one cured by removing egg from the diet. He also believes eczma cannot be made worse by feeding egg. He looks upon infantile eczema as being not exactly an allergic phenomenon but a para-allergic phenomenon going along with allergy, the whole substratum of the process being sensitivity to egg white or egg yolk with, of course, in some cases, primary sensitivity to milk, wheat or any other allergen as the case may be.

Dermatology at present is dominated very much by Bruno Bloch of Zurich and his ideas of eczema. Under his influence the German school confines itself to calling eczema an external dermatitis. A poison ivy or any other external dermatitis is eczema and nothing else is. A good deal of confusion has arisen on that account because in this country the dermatologists have a much broader definition of eczema. The followers of Bloch look upon adult eczema as a contact dermatitis and they determine sensitivity by means of the patch test.

I believe in certain infants we do get sensitivity to external things. I have had patients sensitive to wool, silk, cat fur, dog hair or what not, but I believe the vast majority of reactions come from the ingestion. There are no metabolic changes particularly characteristic of infantile eczema. All metabolic researches have developed nothing of any great moment.

With regard to the use of milk-free diets, Stewart and I some years ago developed Sobee, made of soy bean flour and olive oil, etc., because it seemed we never would be able to tell exactly what rôle milk played in the development of infantile eczema until we could have a satisfactory diet without milk for the baby. I have fed a great many infants on this food and I believe one must not expect too much of it; it is not a cure-all for eczema by any means. If the eczema is due to milk sensitivity, it will undoubtedly be cured by Sobee feeding, provided there are not a great many other sensitivities. If the baby is sensitive to egg and milk and a number of other things, he is not very likely to do well with Sobee feeding. If the eczema is purely and primarily a milk case, the results are very satisfactory. When we first prepared Sobee, we made it of barley flour and later with purified cornstarch on account of the objection Dr. Bell has spoken of. All the Sobee for some time has been made with purified cornstarch and I believe before long arrowroot starch will be used instead, following the suggestion of someone in California.

Certain changes in the protein undoubtedly take place when milk is heated very hot. It is probably true that the lactalbumin is rendered less allergic by prolonged heating. The casein is changed very little. I am skeptical about "denatured" milks. I believe that in some cases of mild milk sensitivity, if the idiosyncrasy is due to lactalbumin alone, the heated milk may do very well but, on the other hand, if the idiosyncrasy is due to both casein and lactalbumin, as it frequently is, or to casein alone, heated milk will not do much and I believe a milk-free diet is very much to be preferred.

I have been able to get very definitely positive skin tests with powdered milk heated to 130° C. for one hour, just as large skin tests as I would with pure casein. I think the subject of heated milk deserves a closer and much more careful study than has been given it as we really know very little about what changes take place in casein when it is heated or indeed if any important changes do take place.

I have had very little experience with either specific or nonspecific desensitization because after studying the literature and talking with a good many people, I concluded it was probably not a very satisfactory procedure for private practice particularly. It takes a good many injections, there may be fairly severe reactions, results are pretty uncertain and if we do get an immunity, it lasts only a comparatively short time. I firmly believe we have no answer to infantile eczema until we have some method of rendering an allergic child nonallergic and that method will come some time in the future through some means of nonspecific therapy. If we have a child with eczema or asthma who has a multiple sensitivity as almost all of them have, it is absurd to expect to cure him by taking away all the things to which he is sensitive or to desensitize him specifically. Much of our treatment of infantile eczema is very crude and some of it rather silly, but I believe we will progress as time goes along.

DR. CHARLES SCHOTT (CHICAGO).—Dr. Schick, have you had any experience with the formic acid injections in eczema?

DR. SCHICK.—We have no experience in eczema though we tried them in asthma. We had some cases which responded to it but we dropped it after a while because the results were not so encouraging.

DR. S. J. LEVIN (DETROIT).—I would like to ask about calcium therapy. I know a great many variable reports have appeared about the value of calcium in eczema and asthma. I have found that calcium given intravenously is of considerable benefit and is something we should give more attention to. In status asthmaticus, we hesitate to use adrenalin continuously because of the short duration of benefit but calcium-gluconate or gluco-calcium given intravenously in amounts up to 10 c.c. has been found to be very effective in controlling these cases; it has helped a great deal in infantile eczema. Whether there is some fundamental calcium imbalance in allergy I do not know. Perhaps there is some disproportion between the calcium and the phosphorus and by elevating the calcium portion, the normal relation between the calcium and phosphorus is obtained. I mention this as a useful practical point in therapy and handling these difficult cases which come in during the pollen season, or cases of status asthmaticus in which the ordinary methods do not seem to help.

Another point I wish to make is the relationship of the skin tests to severity of symptoms especially in cases of pollen asthma. We have found it does not seem to matter much whether positive skin tests are present in large degree, whether they are present only in small degree, or absent entirely. The amount of pollen extract to be given therapeutically is not related in the majority of the cases to the height of the skin reaction. A child with pollen asthma who gives no positive skin tests whatever but whose symptoms occur at the typical pollenating season for

ragweed may be extremely sensitive subcutaneously to the extract of pollen and very minute doses may have to be used. Just the reverse may be true of the patient with extremely large skin reactions.

In any of these pollen cases, the pollen count in the air must be considered. Some men use high amounts of pollen extract and others use very small amounts. One cannot state that a certain amount of pollen is sufficient to cure any case of pollen asthma or hay fever. We have a very high pollen count in Detroit. Kansas City has the highest pollen count in America and Buffalo and Chicago are next; the fourth position is occupied by Detroit. The same patient with the same sensitivity, in an area with a low pollen count does not require many injections, but in the Detroit area we find we need tremendous doses of pollen extract, almost to the point of obliterating the skin tests before we can obtain good relief. We give as a final dose from 1 to 2 c.c. of a 3 per cent solution which is a very strong solution for the average pollen case. On the other hand, we see cases where we can obtain a dosage of only 0.05 c.c. of a 1 in 10,000 solution and still get relief. It is such an individual question and the therapy must be so very detailed and adjusted individually for each patient that I believe one should not make a general rule. Especially, one should not depend too much on height of skin reactions in relation to the size of doses.

I also wanted to talk about the perennial treatment of pollen cases. Dr. Schick is rather opposed to the continuation of perennial therapy and perhaps it does have its disadvantages but, on the other hand, it offers to the patient a possibility of eventually stopping pollen injections. Vaughan of Virginia gives figures indicating 50 per cent cures after three years of continuous therapy. In my own experience, perennial therapy produces what may be called a permanent cure in eighteen months. It is a development in the treatment of allergy which must not be discarded too readily.

The extract of pollen or of foods should not be looked upon as a toxic substance. Whether the reaction of the body against this substance is antitoxic as in the case of diphtheria toxin still has to be shown.

I have seen children subjected to series of elimination diets that produced a very bad constitutional effect with general damage to the child in loss of weight and resistance to disease in the hope that by chance, some food would be eliminated that might be causing the trouble. I believe we should not subject a child to such a serious method of diagnosis in the hope that by chance we will find the cause of their symptoms. It is far more accurate to do the skin tests first and avoid the possibility of injuring the child's general condition by a series of weird diets.

DR. SCHICK.—The following theory about the effect of calcium can be evolved: You remember from the basic experiment of Chiari and Januschke, croton oil put in the conjunctiva of a rabbit's eye produces a tremendous inflammatory reaction. This reaction was suppressed by giving calcium previous to the instillation of croton oil. The linings between the endothelial cells are tightened and made less permeable for exudation. I tried the calcium treatment in many cases and the result was not striking. You can find very much in the literature of twenty years ago about calcium therapy as a preventive measure against hay fever. There is some possibility of influencing the intensity of secretion and of inflammatory reaction on the skin and mucous membrane, but we should not expect a real cure of the condition.

I agree with Dr. Hill that we should not put all the eczemas in one pot.

An hyperergic person is good soil for infections. Secondary infections complicating eczema must be considered. The eczema question is still not entirely solved, and we should be very cautious in our statements.

DR. LEWIS WEBB HILL.—I wish you would say some more about nonspecific therapy in eczema. I know very little about it but feel quite strongly that is what we must have some time if we really want to deal with the disease satisfactorily. This is beside the question of local treatment, of regulating the diet, and taking away something we think the child is sensitive to.

DR. SCHICK.—If we find some causative agents then, of course, these should be taken away, but, I am sure there must be other ways of treatment. If a child gets pneumonia or some other febrile disease, it is astonishing how quickly the eczema disappears and how different the skin looks within seventy-two hours. We do not know what goes on in the system, but we do know that in some way nature is able to make the eczematous reaction disappear.

I have not had much personal experience with the nonspecific treatment and vaccine treatment in eczema. I hesitate to apply this treatment because I feel we are going a little too far in injecting all these different substances.

(Remarks by Dr. Franklin J. Corper, Chicago, not sent in.)

DR. SCHICK.—I wish to express my personal opinion about the perennial treatment. It is possible that interrupted treatment eventually brings about a hypersensitization and perennial treatment prevents it. After interrupted treatment with tuberculin it happens that if one starts over again, one will find the patient more sensitive. I repeat that skin reactivity and asthmatic conditions do not always go parallel. Dr. Peshkin showed me patients with pollen asthma who were absolutely negative to skin tests and still had typical pollen asthma. He could only obtain a positive test by testing the conjunctiva with dry pollen powder. There one sees the dissociation between the reaction of the skin and the reaction of the respiratory tract. The skin is very sensitive and the respiratory tract not so much so. There are also differences which may be explained partly by the different rate of absorption. If a substance is injected subcutaneously, the absorption will be slow; when given into a vein, the absorption is so rapid that a very large amount of this offending substance enters the system at one time.

(Remarks by Dr. I. H. Tumpeer not sent in for publication.)

DR. SCHICK.—It has been my experience that tetanus antitoxin is more toxic than many other therapeutic sera. I have seen the worst kind of serum sickness after injections of tetanus antitoxin. As the purification of tetanus antitoxin is as thorough as that of diphtheria antitoxin, I am unable to explain the difference on that basis. I saw a child whom I had to keep under morphine for three days because of terrific joint pains. There was nothing visible on the joints. Other colleagues reported similar observations to me.

We must differentiate between serum sickness starting after a normal incubation period and one starting after an abnormally short time. If a child develops an intensive serum sickness eight to twelve days after injection, this has nothing to do with a previous sensitizing injection. The whole discussion should deal with the accelerated and immediate reaction.

An important question is whether or not there is danger of an anaphylactic shock in children immunized against diphtheria by toxin antitoxin in case the child must be treated later with a therapeutic serum. Such an occurrence is possible but extremely rare.

Another question I wish to discuss is the reaction observed in older tuberculous children and adults when toxoid (Anatoxin) is used for immunization against diphtheria. The most satisfactory explanation is that tuberculous and other infections

change the general level of sensitivity to foreign protein so that the reaction is different from diphtheria toxin. Infants and children of preschool age show such reactions much less frequently.

We should not go so far as to name everything allergic; this would lead to confusion. I am wondering whether we have the right to explain sudden death in eczema or hyperpyrexia on the basis of hyperergy. The mechanism may be a quite different one and we should look for other explanations.

No child of three or four years will be absolutely free from allergic features. Such features are usually mild, so that they have no special importance. There are different grades of reactivity in different individuals from mild to hyperergic reactions. Hyperergic reactivity has great clinical importance.

DR. MOORE.—I would like to inquire whether there has been a study of defects in the endocrine system of the allergic children. Barber has recently discussed the feeding of glands of internal secretion to certain types of children, the colicky child, the vomiter and I believe to the eczematous child. Has there been any work done on defects of the adrenal as a causative factor?

DR. L. W. HILL.—Would it be possible to settle the question of the danger of anaphylactic shock by looking for precipitins to horse serum in the blood?

DR. SCHICK.—I do not think so. We had the greatest difficulty in finding precipitins in the blood. The human being is a very poor producer of precipitin.

Academy News

The following have been appointed for the Nominating Committee:

Chairman.—Dr. Samuel McC. Hamill, Philadelphia, Pennsylvania
Dr. E. B. Shaw, San Francisco, California
Dr. Hugh Leslie Moore, Dallas, Texas

Dr. Sterling H. Ashmun, of Dayton, Ohio, has been appointed a member of the Ohio State Committee.

News and Notes

International Pediatric Congress*

The third International Pediatric Congress, held in London on July 20-22, under the presidency of Dr. G. F. Still, was attended by nearly 400 delegates from thirty countries. The inaugural ceremony took place in the Great Hall of the British Medical Association House, when T.R.H. the Duke and Duchess of York attended to open the congress and to welcome the members. H.R.H. the Duke of York, in expressing his pleasure at greeting so large a gathering, especially in view of the fact that this was the first international meeting in this country of physicians dealing with the diseases of childhood, made a few well-chosen remarks, stressing the importance of pediatrics particularly on the preventive side. "Speaking as a father," he voiced the gratitude of parents far and wide who would benefit from the deliberations of the congress. The President and Sir Thomas Barlow expressed the thanks of the members to the Duke and Duchess for their interest in the congress and after the departure of the Royal visitors, the scientific proceedings began.

The first main discussion took place on the subject of the nature of allergy and its rôle in diseases of children. Dr. Arnold Rich (Baltimore) spoke from the pathologic side and brought forward the results of experiments which demonstrated that in bacterial allergy the individual tissue cells are hypersensitive to the bacterial antigen and the allergic reaction is not dependent upon circulating antibody. He stressed that all recent work went to show that allergy is not essential for immunity. Experiments show that immunity can be separated from allergy and that neither of the two primary characteristics of immunity—the prevention of spread of bacteria and their efficient destruction—is dependent upon allergic inflammation for successful operation. He further pointed out that allergy be established without immunity and acting alone, it lowers resistance to infection. Professor F. Hamburger (Vienna) dealt more with the clinical aspects of allergy, basing his remarks mainly upon the study of problems of tuberculosis by means of the tuberculin reactions. Allergy could be shown to develop prior to the onset of the disease. It was continuous but subject to the fluctuations caused by other diseases —by light, food and other so far unknown factors; and such fluctuations might be the cause of exacerbations. In his opinion, the tuberculin reaction was of great value in prognosis and tuberculin should be used to a greater extent for prophylaxis. Dr. Pehu (Lyons), in a paper prepared jointly with Dr. P. Woringer (Strasbourg), described the clinical aspects of the allergic states of nonbacterial origin, enumerating the various substances capable of sensitizing the human organism under the main headings of inhalation, food, drug and contact allergens. He proceeded to give a description of the clinical manifestations of the nonbacterial allergic states in the various systems affected, pointing out how the different allergens tended to affect different systems at various periods of life. He thought there were three possible causes of nonbacterial allergy: sensitization after birth, sensitization in utero, and hereditary transmission by the germ cells, the last being of a specific nature or merely the inheritance of a predisposition. Dr. W. R. F. Collis (Dublin) advanced the view that the same disease syndrome could be pro-

*British Med. J., July 29, 1933.

duced by more than one organism provided that the body was in the state of allergy, and he instanced erythema nodosum in this connection. Dr. H. Ernberg (Stockholm) also discussed allergy in relation to erythema nodosum. Professor F. Groer (Lwow) stressed the kinetic aspects of allergy, dependent upon two main factors—the susceptibility of the body and the power to react on the part of the body. He explained how these factors could be assessed accurately in the case of a disease such as tuberculosis. Professor G. de Toni (Bologna), Professor R. Debré (Paris) and Dr. B. Ratner (New York) also took part in the discussion.

The discussion of the second day, on the prophylaxis of milk-borne diseases, was opened by Professor A. Pettersson (Stockholm) who dealt especially with the problem of tuberculosis. Not only was there the universal danger of bovine tuberculosis but in the speaker's opinion, human tubercle were frequently introduced into the human body with milk. He also mentioned the risk of infection with the organisms of undulant fever in those districts where infectious abortion occurred, but children under ten years of age fortunately appear to be either insusceptible or very slightly susceptible. Professor G. Bessau (Berlin) spoke of the saprophytic organisms in milk and their significance. The introduction of varieties of the colon bacillus by milk into the alimentary canal in children produced a completely different type of intestinal flora from that in the breast-fed baby, for example, and many of the digestive disturbances in the artificially fed baby could be attributed to the spread of Bacillus coli to the upper parts of the alimentary tract. In contrast to the adult, where the presence of the coli bacilli in the bowel had no deleterious effects, young babies might develop inflammation of the whole of the intestine, small and large, from this cause. Professor G. B. Allaria (Turin) explained that in Italy at present there was a strong movement for the improvement of the dairy industry and in the meanwhile, it was of importance to seek an answer to the question of whether the advantages of giving raw milk as a "live" liquid and attempting to prevent bacterial contamination were greater than those obtained by giving a sterile milk at the expense of its vital properties. The speaker thought that the importance of the vital properties had been exaggerated and that in the present state of the dairy industry in the majority of countries, the only course was to purify the milk by some thermic process. Professor P. Lereboullet (Paris) brought forward a survey of the possibilities of diminishing the risks from cow's milk by a thoroughly planned hygienic scheme by legislation and by municipal and collective measures. He summarized the position in certain countries and stressing especially the difficulties, concluded strongly in favor of pasteurization of milk under proper control as the ideal measure. Failing a proper organization, he thought the boiling of milk prior to consumption was the only course. Dr. J. M. Hamill (London), gave a short review of the position in this country as regards bovine tuberculous infection in children. Since, as he pointed out, even certified and tuberculin-tested milk occasionally contained tubercle bacilli, there was no alternative to some treatment of the milk to destroy organisms. This, he thought, was to be found in efficiently controlled pasteurization. He emphatically condemned the idea that the drinking of infected milk was valuable to produce an immunity. The discussion was continued by Professor F. Feer (Zurich), Professor S. Monrad (Copenhagen), Professor P. Rohmer (Strasbourg), Professor G. Frontali (Padua), Dr. H. Bock (Berlin), Dr. W. C. Davison (U. S. A.), Dr. H. P. Wright (Montreal), Dr. J. Duzar (Pecs), Professor G. Mouriquand (Lyons), Professor G. Noeggerath (Freiburg), Dr. W. Spolverini (Rome), Professor W. I. Jundell (Stockholm) and Dr. G. Petranzi (Hungary).

The afternoon sessions on the first two days and the morning session on the last day were devoted to short communications given in sectional meetings. On the social side the delegates were offered an excellent series of gatherings. On Thursday,

July 20, the Royal College of Physicians gave a reception at which the guests were welcomed by Lord and Lady Dawson. Later in the evening Dr. G. F. Still held a presidential reception at the Goldsmiths' Hall where the guests were received by Lord Queenborough. Academic robes were worn and the magnificent possessions of the Goldsmiths' Company were exhibited to a large gathering, marked by the wealth of color of the gowns of the delegates. On Friday, July 21, Lord and Lady Howard de Walden gave an afternoon reception, while in the evening the dinner of the congress was held at the May Fair Hotel. At this ceremony, after "The International Congress" and "The Guests" had been proposed by the chairman (Dr. G. F. Still), the Minister of Health (Sir Hilton Young) replied on behalf of the latter. "The Chairman's Health" was proposed by Sir Thomas Barlow. The delegates afterward proceeded to a reception by H. M. Government at Lancaster House, where Sir Hilton and Lady Young welcomed the visitors.

On the afternoon of the last day a clinical demonstration of patients from the London hospitals was held at the Hospital for Sick Children, Great Ormond Street, and after this, a reception by Sir Gomer and Lady Berry took place at the Infants Hospital, Vincent Square. The next congress will be held in Rome in 1936, under the presidency of Dr. L. Spolverini.

Notes

Friends of Professor G. F. Still have undertaken to recognize the occasion of his retirement from active direction of the Great Ormond Street Hospital for Sick Children in London. It has been proposed that a bed be named for him at Kings College Hospital and to show other signs of appreciation of his distinguished service to pediatrics not only in Great Britain but throughout the world. Subscriptions to a fund to establish such a tribute to Professor Still has been undertaken by various organizations in England, Canada, and in this country.

Graduate courses in pediatrics for physicians have been announced by New York Post Graduate Medical School of Columbia University and by the School of Medicine of Washington University, St. Louis.

The course at New York Post Graduate Medical School begins October 4, 1933, and continues for nine weeks, to November 29, 1933. It will be given under the direction of Professor Roger H. Dennett. The course is designed to cover most of the essentials of pediatrics and is planned to meet the needs of physicians in northern New Jersey, southern New York and Connecticut or those residing within two hours' travel of New York City without materially interfering with their daily home practice.

The course at Washington University, St. Louis, is under the direction of Dr. W. McKim Marriott and consists of an intensive full-time course in pediatrics at the St. Louis Children's Hospital. The course begins October 2, 1933.

Comments

LIFE has become a complicated matter for the young child. Time was when he "just grew." If his parents could afford it he had a nurse-maid, perhaps a foster-mother, and the family doctor occasionally lent a hand for ailments beyond the healing range of the castor oil bottle; but on the whole there wasn't much to disturb the even tenor of his ways. He had his measles and whooping cough, to be sure, and maybe scarlet fever, and survived them (or not) mainly by grace of Mother Nature. If he had rickets nobody knew it, and he lived in blissful ignorance of shots in the arm. He was even allowed to keep his tonsils.

We pediatricians have changed all that. First we learned to calculate just how much food he needs, and to be sure he gets it with proper exactitude, we have impressed on his mother the importance of carefully measured amounts at stated intervals. If the baby happens to want to sleep when he should be feeding, or would like more at one meal and less at another, that's his hard luck.

Having solved the feeding problem, eager for more worlds to conquer, we have found a growing list of diseases to prevent. The babe goes in imminent danger of rickets, scurvy, smallpox, diphtheria, measles, scarlet fever, whooping cough, poliomyelitis; not to mention the common cold and sore throat. Some of these can be warded off by more or less unpleasant drugs or a few hypodermics; others we're not so sure about but a shot or so may be worth trying. Tonsils and adenoids are a nuisance anyway. Out with them! Sunshine is the great cure-all. Baby must have it. Of course the best sunshine comes in the hottest weather, when he might prefer to stay in the shade; no matter, off with his clothes and out in the sun he goes. If it makes him a little cross at first, he'll get over it, and the coat of tan he acquires is a sure sign that he has been protected from something. In the dark months a daily dose of the "sun lamp" can be added to the regimen. And the vitamins must not be forgotten—the irradiated foods, the iodine that wards off goiter; and perhaps a little iron in his milk might be advisable. It's nice that we don't have to depend on natural foods any more.

Of course, this complicated régime not only includes but demands the regular, frequent supervision of the pediatrician, and each of his visits is likely to involve the laying down of a few new rules for baby's guidance. It wouldn't be fair to say that this is merely to justify the pediatrician's presence, for the mother and nurse have learned to demand it.

The pediatrician and the nurse do not always have things their own way. Sometimes the babe rebels at his well-ordered existence and says he won't eat his spinach or drink the right amount of milk. This calls for the child psychologist or even the psychiatrist. The whole family may need to be psychoanalyzed. Another unit has been added to the baby's staff and more complications have come into his life. Perhaps the nursery school may help to teach him conformity.

The pediatrician, though he may have been the prime mover, is not directly responsible for all this. No well-conducted newspaper nowadays would let a day go by without a column or so to impress upon the mother the number of things she ought to be doing for her child. Each of her circle of friends can add something wonderful that she knows.

Seriously, one comes to wonder at times just how many of the things that we have introduced into the child's life are real necessities, or actual improvements over the good old ways; and one might well ask oneself just how much chance there is, in the family that can afford all the frills, for the child to have what might be called a natural development. Or are our children really better for having the years once given over to irresponsible play all cut to pattern?

There is a large class of well-to-do mothers whose care of their children seems to be governed by fads—fads in doctors, fads in schools, fads in foods; in other words, the baby is becoming a fad, and in this day of fads it's not surprising. The writer sometimes thinks that he would like to initiate a new fad whose slogan should be: "Give the poor kid a chance."

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